PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF
THE EDITORIAL COMMITTEE

HONORARY EDITORS:
MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH
SESSION 1946-47

NOVEMBER, 1946—DECEMBER, 1947

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Edited Under the Direction of the EDITORIAL COMMITTEE

Honorary Editors: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.

Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

OFFICERS:

President—Sir Maurice Cassidy, K.C.V.O., M.D.

Immediate Past-President—Sir Gordon Gordon-Taylor, K.B.E., M.S.

Vice-Presidents—(Being the Presidents or duly appointed Representatives of the Sections the names of which are given in brackets)—Stanley Rowbotham, M.D. (Anæsthetics); A. Dickson Wright, M.S. (Clinical); G. R. Cameron, F.R.C.P., F.R.S. (Comparative Medicine); M. Sydney Thomson, M.D. (Dermatology); L. R. Broster, O.B.E., M.Ch. (Endocrinology); H. J. Parish, M.D. (Epidemiology and State Medicine); H. P. Himsworth, M.D. (Experimental Medicine and Therapeutics); Sir Arthur MacNalty, K.C.B., M.D. (History of Medicine); Norman Patterson, F.R.C.S. (Laryngology); Maurice Davidson, M.D. (Medicine); Douglas McAlpine, M.D. (Neurology); James Wyatt, F.R.C.S. (Obstetrics and Gynæcology); H. Stobie, F.R.C.S., L.D.S.E. (Odontology); Harold Levy, F.R.C.S. (Ophthalmology); V. H. Ellis, F.R.C.S. (Orthopædics); H. V. Forster, M.C., M.B. (Otology); Denis Browne, F.R.C.S. (Pædiatrics); A. B. Rosher, (Pathology); Frank Cooksey, O.B.E., M.D. (Physical Medicine); A. Hedley Whyte, M.S. (Proctology); Aubrey Lewis, M.D. (Psychiatry); Hugh Davies, D.M. (Radiology); Sir James Walton, K.C.V.O., M.S. (Surgery); R. H. O. B. Robinson, F.R.C.S. (Urology).

Honorary Treasurers—J. B. Hunter, C.B.E., M.Ch.; C. E. Newman, M.D.

Honorary Librarians—E. K. Martin, M.S.; T. C. Hunt, D.M.

Honorary Secretaries—R. H. O. B. Robinson, F.R.C.S.; W. A. Pool, M.R.C.V.S.

Honorary Editors—Maurice Davidson, M.D.; Eric A. Crook, M.Ch.

Other Members of Council—Alice Bloomfield, F.R.C.S.; E. R. Boland, C.B.E., F.R.C.P.; L. R. Broster, O.B.E., M.Ch.; E. A. Cockayne, D.M.; V. Zachary Cope, M.S.; Macdonald Critchley, M.D.; E. R. Cullinan, M.D.; R. Davies-Colley, C.M.G., M.Ch.; Anthony Feiling, M.D.; Sir Archibald Gray, C.B.E., M.D.; Charles Harris, M.D.; H. L. Marriott, C.B.E., F.R.C.P.; Geoffrey Marshall, O.B.E., M.D.; M. F. Nicholls, C.B.E., M.Ch.; A. C. Roxburgh, M.D.; Sir Henry Tidy, K.B.E., M.D.

NON·EST·VIVERE
SED·VALERE·VITA

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.

ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

OFFICERS:

President—Sir Maurice Cassidy, K.C.V.O., M.D.

Immediate Past-President—Sir Gordon Gordon-Taylor, K.B.E., M.S.

Vice-Presidents—(Being the Presidents or duly appointed Representatives of the Sections the names of which are given in brackets)—Stanley Rowbotham, M.D. (Anæsthetics); A. Dickson Wright, M.S. (Clinical); G. R. Cameron, F.R.C.P., F.R.S. (Comparative Medicine); M. Sydney Thomson, M.D. (Dermatology); L. R. Broster, O.B.E., M.Ch. (Endocrinology); H. J. Parish, M.D. (Epidemiology and State Medicine); H. P. Himsworth, M.D. (Experimental Medicine and Therapeutics); Sir Arthur MacNalty, K.C.B., M.D. (History of Medicine); Norman Patterson, F.R.C.S. (Laryngology); Maurice Davidson, M.D. (Medicine); Douglas McAlpine, M.D. (Neurology); James Wyatt, F.R.C.S. (Obstetrics and Gynæcology); H. Stobie, F.R.C.S., L.D.S.E. (Odontology); Harold Levy, F.R.C.S. (Ophthalmology); V. H. Ellis, F.R.C.S. (Orthopædics); H. V. Forster, M.C., M.B. (Otology); Denis Browne, F.R.C.S. (Pædiatrics); A. B. Rosher, (Pathology); Frank Cooksey, O.B.E., M.D. (Physical Medicine); A. Hedley Whyte, M.S. (Proctology); Aubrey Lewis, M.D. (Psychiatry); Hugh Davies, D.M. (Radiology); Sir James Walton, K.C.V.O., M.S. (Surgery); R. H. O. B. Robinson, F.R.C.S. (Urology).

Honorary Treasurers—J. B. Hunter, C.B.E., M.Ch.; C. E. Newman, M.D.

Honorary Librarians—E. K. Martin, M.S.; T. C. Hunt, D.M.

Honorary Secretaries—R. H. O. B. Robinson, F.R.C.S.; W. A. Pool, M.R.C.V.S.

Honorary Editors—Maurice Davidson, M.D.: Eric A. Crook, M.Ch.

Other Members of Council—Alice Bloomfield, F.R.C.S.; E. R. Boland, C.B.E., F.R.C.P.; L. R. Broster, O.B.E., M.Ch.; E. A. Cockayne, D.M.; V. Zachary Cope, M.S.; Macdonald Critchley, M.D.; E. R. Cullinan, M.D.; R. Davies-Colley, C.M.G., M.Ch.; Anthony Feiling, M.D.; Sir Archibald Gray, C.B.E., M.D.; Charles Harris, M.D.; H. L. Marriott, C.B.E., F.R.C.P.; Geoffrey Marshall, O.B.E., M.D.; M. F. Nicholls, C.B.E., M.Ch.; A. C. Roxburgh, M.D.; Sir Henry Tidy, K.B.E., M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

JOINT DISCUSSIONS

SECTION OF MEDICINE WITH SECTION OF PHYSICAL MEDICINE
(*JOINT DISCUSSION No.* 1)

January 28, 1947

	PAGE *Section*	*Volume*
THE ÆTIOLOGY OF CHRONIC RHEUMATISM	—	329–346
Dr. W. S. C. Copeman	—	329
Dr. Philip Ellman	—	332
Dr. G. D. Kersley	—	343
Dr. Ernest Fletcher, Dr. W. R. Thrower, Dr. W. Annandale Troup	—	345
Dr. W. Ganado	—	346

SECTION OF SURGERY WITH SECTION OF RADIOLOGY
(*JOINT DISCUSSION No.* 2)

January 1, 1947

DISCUSSION ON THE TREATMENT OF CANCER OF THE TONGUE	—	409–418
Sir Stanford Cade	—	409
Dr. Ralston Paterson	—	412
Mr. W. R. Douglas	—	415
Lieut.-Colonel W. L. Harnett	—	417
Mr. Anthony Green	—	418

SECTION OF OBSTETRICS AND GYNÆCOLOGY WITH SECTION OF RADIOLOGY
(*JOINT DISCUSSION No.* 3)

May 16, 1947

DISCUSSION ON SOME ASPECTS OF SURGICAL AND RADIOLOGICAL TREATMENT OF CARCINOMA OF THE CERVIX	—	907–922
Professor Subodh Mitra, F.R.C.S.Ed., F.R.C.O.G. (*Calcutta*)	—	907
Mr. Charles D. Read	—	909
G. E. Richards, M.D. (Toronto) *	—	911
Mr. G. W. Blomfield	—	917
Mr. Frank Cook	—	922

* *See also* Vol. 41, p. 150.

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Edited Under the Direction of the EDITORIAL COMMITTEE
Honorary Editors: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF ANÆSTHETICS

OFFICERS:

President—Stanley Rowbotham, M.D.

Vice-Presidents—George Edwards; Frankis Evans, M.B.; R. J. Minnitt, M.D.

Hon. Secretaries—W. A. Low, M.C., M.B.; John Gillies, M.C., F.R.C.S.Ed.

Other Members of Council—A. H. Galley; R. Blair Gould, M.B.; T. Cecil Gray, M.B.; Ronald Jarman, D.S.C.; K. G. Lloyd-Williams, M.D.; A. D. Marston; H. J. V. Morton, M.D.; W. W. Mushin, M.B.; M. D. Nosworthy, M.D.; G. S. W. Organe, M.D.; F. W. Roberts, M.B.

Representative on Library Committee—C. F. Hadfield, M.B.E., M.D.

Representative on Editorial Committee—J. Blomfield, O.B.E., M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Anæsthetics

CONTENTS

December 6, 1946

	PAGE *Section*	*Volume*
DISCUSSION : SHOCK WITH SPECIAL REFERENCE TO ANÆSTHESIA	1–12	167–178
Professor H. N. Green	1	167
Dr. R. P. Harbord	6	172
Dr. R. J. Minnitt, Dr. Ronald Woolmer, Dr. Barnet Solomons	11	177
Dr. H. W. Loftus Dale, Dr. Stanley Rowbotham, Dr. R. P. Harbord, Professor H. N. Green	12	178

January 3, 1947

DISCUSSION : ANÆSTHESIA FOR ABDOMINO-PERINEAL OPERATIONS FOR CANCER OF THE RECTUM	13–20	263–270
Dr. Ronald Jarman	13	263
Dr. Frankis Evans	16	266
Mr. O. V. Lloyd-Davies	18	268
Dr. V. Eades Vessell, Dr. H. W. Loftus Dale, Dr. Victor Goldman	19	269
The President (Dr. Stanley Rowbotham), Dr. Frankis Evans	20	270

March 7, 1947

DISCUSSION ON LOCAL ANALGESIA	21–28	525–532
Dr. Norman R. James	21	525
Dr. Frederick Prescott	23	527
Mr. H. W. L. Molesworth	25	529
Dr. F. W. Roberts, Dr. S. G. Ransom, Mr. Harold Dodd	27	531
Dr. Stanley Rowbotham	28	532

April 11, 1947

DISCUSSION ON FURTHER EXPERIENCES WITH CURARE	29–38	593–602
Dr. Frederick Prescott (*in absentia*, read by Dr. R. H. Roberts)	29	593
Dr. Geoffrey Organe	32	596
Dr. Barnett Mallinson	34	598
Dr. A. C. Forrester, Dr. John Gillies	36	600
Dr. John Halton, Dr. L. O. Mountford, Dr. H. B. Wilson, Dr. Massey Dawkins, Dr. Cecil Gray	37	601
Dr. Barnett Mallinson	38	602

May 2, 1947

CONTROLLED RESPIRATION BY MEANS OF SPECIAL AUTOMATIC MACHINES AS USED IN SWEDEN AND DENMARK. [*Abstract*] E. Trier Moerch, M.B., B.S., M.D.Copenhagen	39	603
SKIN TEMPERATURE AS A CLINICAL AID DURING ANÆSTHESIA. [*Abridged*] J. Clutton-Brock, M.B., D.A.	43	607

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

CLINICAL SECTION

OFFICERS:

President—A. DICKSON WRIGHT, M.S.

Vice-Presidents—CLIVE BUTLER, F.R.C.S.; KENNETH HERITAGE, F.R.C.S.; R. VAUGHAN HUDSON, F.R.C.S.; WILFRED STOKES, M.D.; PHILIP TURNER, M.S.; A. L. WINGFIELD, M.D.

Hon. Secretaries—G. E. VILVANDRÉ; T. W. MIMPRISS, M.S.

Other Members of Council—R. R. BOMFORD, F.R.C.P.; R. C. BROCK, M.S.; A. P. CAWADIAS, O.B.E., M.D.; E. A. COCKAYNE, M.D.; F. D'ABREU, F.R.C.S.; A. ELKELES, M.D.; HORACE EVANS, M.D.; LEONARD FINDLAY, M.D.; F. P. FITZGERALD, F.R.C.S.; DUNCAN FITZWILLIAMS, C.M.G., F.R.C.S.; CLIFFORD HOYLE, M.D.; REGINALD A. KING, F.R.C.S.; IVOR LEWIS, M.S.; LEO RAU, M.D.; J. S. RICHARDSON, M.V.O., M.D.; MICHAEL J. SMYTH, M.Ch.; HUGH STANNUS, M.D.; HERMON TAYLOR, F.R.C.S.

Representative on Library Committee—NEILL HOBHOUSE, M.D.

Representative on Editorial Committee—J. S. RICHARDSON, M.V.O., M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7 CLIFFORD STREET, W.1.
1947

Clinical Section

CONTENTS

October 11, 1946

	PAGE Section	 Volume
Bone Deformity Associated with Multiple Neurofibromatosis Norman C. Tanner, F.R.C.S.	1	47
Ligation of the Inferior Vena Cava for Femoral Thrombosis with Pulmonary Infarction J. D. Fergusson, M.D., F.R.C.S.	3	49
Von Recklinghausen's Disease A. Dickson Wright, M.S., F.R.C.S.	3	49
Total Gastrectomy with Œsophagoduodenal Anastomosis A. Dickson Wright, M.S., F.R.C.S.	4	50

November 8, 1946

	Section	Volume
Myelosclerosis with Leukæmoid Blood Picture E. Idris Jones, M.D.	5	117
Xanthomatosis C. P. Petch, M.B., M.R.C.P. (for Professor de Wesselow, D.M., F.R.C.P.)	6	118
Sarcoma of Bronchus Ivor Lewis, M.S.	7	119
Neurofibroma of Stomach in Von Recklinghausen's Disease T. W. Mimpriss, M.S.	8	120
Cirsoid Aneurysm K. W. Priddis, F.R.C.S. (for Mr. Alan Small)	9	121

December 13, 1946

	Section	Volume
Paterson-Plummer-Vinson Syndrome in a Case of Familial Acholuric Jaundice Leo Rau, M.D., M.R.C.P.	11	271
Tendon Transplantation for Posterior Interosseous Nerve Paralysis Reginald A. King, O.B.E., F.R.C.S.	12	272
Leontiasis Ossea J. M. Willcox, M.B. (for Ivor Lewis, M.S., M.D.)	13	273
Malignant Synovioma of the Left Elbow Ralph Shackman, F.R.C.S.	13	273
Transthoracic Partial Gastrectomy for Intussuscepted Fibromyoma of Fundus of Stomach Norman C. Tanner, F.R.C.S.	15	275
Two Cases of Transthoracic Gastrectomy Norman C. Tanner, F.R.C.S.	16	276

February 14, 1947

PAGE
Volume

SCLERODACTYLIA WITH ŒSOPHAGEAL LESION (3 CASES)
William A. Bourne, M.D., M.R.C.P. 463

ŒSOPHAGEAL CARCINOMA TREATED BY RESECTION AND PRESTERNAL ŒSOPHAGO-GASTROSTOMY
Hermon Taylor, F.R.C.S. 465

OSTEOPOROSIS CIRCUMSCRIPTA AND LEONTIASIS OSSEA FACIEI ASSOCIATED WITH PAGET'S DISEASE
A. Elkeles, M.D. 466

March 14, 1947

LYMPHADENOMA
Leo Rau, M.D. 468

HYPOTHYROIDISM WITH MACULAR ABIOTROPHY AND INNER EAR DEAFNESS
Leo Rau, M.D. 468

LARGE CHRONIC RODENT ULCER TREATED BY RADIOTHERAPY
J. A. C. Fleming, F.R.C.S.Ed. 469

ARTERIOVENOUS FISTULA WITHOUT A HISTORY OF TRAUMA
C. G. Rob, M.Ch., F.R.C.S. 470

MALIGNANT LYMPHO-ENDOTHELIOMA OF NECK
T. W. Mimpriss, M.S. 471

May 9, 1947

WOLFF-PARKINSON-WHITE SYNDROME (SHORT P-R INTERVALS ASSOCIATED WITH DISTURBANCES OF INTRAVENTRICULAR CONDUCTION) WITH ATTACKS OF PAROXYSMAL TACHYCARDIA IN AN INFANT AGED 8 MONTHS SUFFERING FROM PROBABLE CONGENITAL HEART DISEASE
A. Schott, M.D. 472

DERMATOMYOSITIS
W. E. Clarke, M.R.C.P. (for E. C. Warner, F.R.C.P.) 475

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by
Staples Press Limited
at their
Great Titchfield Street, London, establishment

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF COMPARATIVE MEDICINE

OFFICERS:

President—G. R. CAMERON, F.R.C.P., F.R.S.

Immediate Past-President—W. A. POOL, M.R.C.V.S.

Vice-Presidents—V. D. ALLISON, M.D.: J. T. EDWARDS, M.R.C.V.S.; Sir ALEXANDER FLEMING, F.R.C.S., F.R.S.; R. E. GLOVER, F.R.C.V.S.; R. LOVELL, F.R.C.V.S.; C. L. OAKLEY, M.D.; A. W. STABLEFORTH, M.R.C.V.S.; E. G. WHITE, M.R.C.V.S.

Hon. Secretaries—A. HADDOW, M.D.; W. M. HENDERSON, D.Sc.

Other Members of Council—J. M. ALSTON, M.R.C.P.Ed.; C. H. ANDREWES, M.D., F.R.S.; S. P. BEDSON, M.D., F.R.S.; J. B. BROOKSBY, M.R.C.V.S.; M. CRAWFORD, M.R.C.V.S.; ROBERT CRUICKSHANK, M.D.; Sir WELDON DALRYMPLE-CHAMPNEYS, Bt., F.R.C.P.; H. H. GREEN, D.Sc.; H. GRÜNEBERG, M.D.; J. E. McCARTNEY, M.D.; DOUGLAS McCLEAN, M.B.; A. A. MILES, F.R.C.P.; WILSON SMITH, M.D.; W. R. WOOLDRIDGE, M.R.C.V.S.

Representative on Library Committee—W. A. POOL, M.R.C.V.S.

Representative on Editorial Committee—C. L. OAKLEY, M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Comparative Medicine

CONTENTS

October 16, 1946

	PAGE Section	PAGE Volume
SUDDEN SHIFTS OF BODY FLUIDS President's Address by Professor G. R. Cameron, F.R.C.P., F.R.S. ..	1	1

December 4, 1946

	PAGE Section	PAGE Volume
STUDIES ON THE HÆMATOLOGY OF THE HORSE, OX AND SHEEP H. H. Holman, D.Sc., Ph.D., M.R.C.V.S.	7	185
THE SERUM PROTEINS OF THE DOMESTIC ANIMALS John B. Brooksby, M.R.C.V.S...	9	187
THE CONSTITUENTS OF NORMAL HUMAN BLOOD C. L. Oakley, M.D.	12	190
INHERITED DISORDERS OF THE BLOOD IN RODENTS Hans Grüneberg, M.D.	13	191

February 19, 1947

	PAGE Section	PAGE Volume
TERATOMAS AND MIXED TUMOURS IN ANIMALS AND THEIR BEARINGS ON HUMAN PATHOLOGY. [*Summary*] Professor R. A. Willis	15	635
SOME GLANDULAR TUMOURS OF THE DOG E. Cotchin, M.R.C.V.S...	16	636

March 19, 1947

	PAGE Section	PAGE Volume
DISCUSSION ON THE SPAN OF LIFE	18–24	638–644
Sir Edward J. Salisbury	18	638
Dr. John Hammond	21	641
Dr. V. Korenchevsky, Dr. Muriel Robertson..	23	643
Dr. R. E. Rewell	24	644

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF DERMATOLOGY

OFFICERS:

President—M. SYDNEY THOMSON, M.D.

Past-Presidents (ex-officio)—H. G. ADAMSON, M.D.; Sir ERNEST GRAHAM-LITTLE, M.D.; J. H. SEQUEIRA, M.D.; J. M. H. MACLEOD, M.D.; S. ERNEST DORE, M.D.; Sir ARCHIBALD GRAY, C.B.E., M.D.; HENRY MACCORMAC, C.B.E., M.D.; H. W. BARBER, F.R.C.P.; H. HALDIN-DAVIS, F.R.C.S.; W. J. O'DONOVAN, O.B.E., M.D.; H. C. SEMON, M.D.; A. C. ROXBURGH, M.D.

Vice-Presidents—W. HERBERT BROWN, M.D.; H. THOMPSON BARRON, M.D.; G. B. DOWLING, M.D.; W. DYSON, M.D.; R. HALLAM, M.D.; J. T. INGRAM, M.D.; F. PARKES WEBER, M.D.; J. E. M. WIGLEY, M.B.

Hon. Secretaries—C. H. WHITTLE, M.D.; F. R. BETTLEY, M.R.C.P.

Other Members of Council—R. T. BRAIN, M.D.; A. BURROWS, M.D.; GEOFFREY DUCKWORTH, M.R.C.P.; W. N. GOLDSMITH, M.D.; R. M. B. MACKENNA, M.D.; P. B. MUMFORD, M.D.; B. C. TATE, M.B.E., M.D.; E. W. PROSSER THOMAS, M.D.; H. R. VICKERS, M.R.C.P.

Representative on Library Committee—GEOFFREY DUCKWORTH, M.R.C.P.

Representative on Editorial Committee—E. W. PROSSER THOMAS, M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W 1.
1947

Section of Dermatology

CONTENTS

October 17, 1946

	PAGE Section	PAGE Volume
CASE FOR DIAGNOSIS. ? LICHEN PLANUS HYPERTROPHICUS C. H. Whittle, M.D.	1	7
HÆMORRHAGIC TELANGIECTASIA OF RENDU-OSLER-WEBER, WITH NO FAMILY HISTORY C. H. Whittle, M.D.	1	7
HÆMORRHAGIC TELANGIECTASIA OF RENDU-OSLER-WEBER C. H. Whittle, M.D.	1	7
DARIER'S DISEASE AND GENERALIZED PRURITIS Louis Forman, M.D.	2	8
CASE FOR DIAGNOSIS. ? LICHEN SCLEROSUS H. J. Wallace, M.D.	2	8
KERATODERMA PALMARIS ET PLANTARUS G. C. Wells, M.R.C.P. (for H. J. Wallace, M.D.)	3	9
LICHEN NITIDUS J. R. Simpson, M.B. (for H. J. Wallace, M.D.)	3	9
EFFECT OF CALCIFEROL ON LUPUS VULGARIS (TWO CASES), LUPUS PERNIO AND BOECK'S SARCOID I. R. Marre, L.R.C.P., M.R.C.S.	4	10
SARCOIDOSIS TREATED WITH CALCIFEROL Brian Russell, M.D.	6	12
CASE FOR DIAGNOSIS. ? RETICULOSIS. ? CIRCUMSCRIBED MYXŒDEMA Brian Russell, M.D.	6	12
MILIARY LYMPHOCYTOMA F. R. Bettley, M.R.C.P.	7	13
DERMATITIS BULLOSA STRIATA PRATENSIS H. Gruebel Lee, M.B., Ch.B. (introduced by Dr. I. Muende)	8	14

November 21, 1946

	PAGE Section	PAGE Volume
ULCER OF VULVA IN YOUNG GIRL M. Moore White, M.D. (by kind permission and in conjunction with R. T. Brain, F.R.C.P.)	9	243
MULTIPLE TUBERCULIDES, INCLUDING THE SCLERODERMA-LIKE FORM OF ERYTHEMA INDURATUM H. W. BARBER, M.B.	11	245
EXFOLIATIVE ERYTHRODERMIA WITH MARKED PIGMENTATION J. E. M. Wigley, M.B.	12	246
IMPETIGO HERPETIFORMIS. ? PEMPHIGUS VEGETANS J. E. M. Wigley, M.B.	14	248
PAPULO-NECROTIC TUBERCULIDES Louis Forman, M.D.	14	248
LEIOMYOMA CUTIS G. B. Mitchell-Heggs, O.B.E., F.R.C.P., and M. H. Small, M.R.C.S., L.R.C.P.	15	249
ERYTHRODERMIA IN LYMPHATIC LEUKÆMIA (MALIGNANT ERYTHRODERMIA) G. B. Mitchell-Heggs, O.B.E., F.R.C.P., H. Corsi, F.R.C.S., and K. D. Crow, M.R.C.P.	15	249
? EPIDERMODYSPLASIA OF LEWANDOWSKI AND LUTZ. ? ABORTIVE FORM OF BLASTOMYCOSIS OR CHROMOBLASTOMYCOSIS H. W. Allen, D.M.	17	251
A HEREDITARY ECTODERMAL DYSPLASIA, HITHERTO NOT DESCRIBED, INCLUDING GROUPED COMEDONES C. H. Whittle, M.D.	17	251
? KAPOSI'S VARICELLIFORM ERUPTION C. H. Whittle, M.D.	18	252
LUPUS VULGARIS AND TUBERCULIDES OF FACE Bernard Green, M.R.C.S., L.R.C.P.	19	253
CUTANEOUS PAPILLOMATOSIS R. M. B. MacKenna, M.D., and Brian Russell, M.D.	20	254

PAGE
Section Volume

December 19, 1946

ERYTHEMATOUS INITIAL TUBERCULIDE
W. J. Hohmann, M.D., Groningen, Holland 21 255

Myxœdema Circumscriptum
W. Freudenthal, M.D. 24 258

Nodules in Abdominal Wall for Diagnosis. ? Fibrosarcoma (Darier and Ferrand)
A. C. Roxburgh, M.D. 25 259

Polymorphic Light Eruption
F. Ray Bettley, M.D. 27 261

Hyperkeratosis Follicularis et Parafollicularis in Cutem Penetrans (*Kyrle*)
J. R. Simpson, M.B. 28 262

January 16, 1947

Lichen Planus in a Boy Aged 8 Years
H. Corsi, F.R.C.S. 29 477

Hyperkeratotic Systematized Nævus with ? Bromide Eruption
A. Hargreaves, M.B. (for W. N. Goldsmith, M.D.) 29 477

Pityriasis Rubra Pilaris
G. B. Mitchell-Heggs, O.B.E., F.R.C.P., and M. Feiwel, M.B. 31 479

? Poikiloderma ? Premycosis
G. B. Mitchell-Heggs, O.B.E., F.R.C.P. 32 480

Pili Torti
G. B. Mitchell-Heggs, O.B.E., F.R.C.P., and W. R. May, M.B., B.S. .. 33 481

Dermatomyositis in a Child
Doyne Bell, D.M. 33 481

Recurrent Ulcers of the Legs
G. C. Wells, M.R.C.P. 34 482

Leukæmia Cutis ? Myeloid Leukæmia
E. Colin Jones, M.B. 35 483

Lupus Vulgaris with Epithelioma and Mutilations
G. B. Mitchell-Heggs, O.B.E., F.R.C.P., and J. R. Owen, M.R.C.P. .. 36 484

February 20, 1947

Granulosis Rubra Nasi
D. I. Williams, M.B. (for Sydney Thomson, M.D.) 37 499

Poikiloderma Congenitale (Thomson). Two Cases
C. H. Whittle, M.D. 37 499

Raynaud's Phenomenon, with Paroxysmal Hæmoglobinuria, Caused By Cold Hæmagglutination
C. H. Whittle, M.D., A. Lyell, M.B., and M. Gatman, M.B... .. .. 38 500

Tropical Lichenoid Dermatitis
H. J. Wallace, M.D. 40 502

Mycosis Fungoides—Treated with Thorium X
Bernard Green, M.R.C.S., L.R.C.P. 41 503

Mycosis Fungoides
Bernard Green, M.R.C.S., L.R.C.P. 42 504

Mycosis Fungoides
J. R. Owen, M.R.C.P. 43 505

Blue Nævus in a Mongolian Patch
C. L. Collins, M.B. 43 505

Morphœa Guttata
Brian Russell, M.D. 44 506

Leucoderma and Leucotrichia
Brian Russell, M.D. 44 506

? Lupus Vulgaris
E. Colin Jones, M.B. 44 506

Favus
E. Colin Jones, M.B. 44 506

Section of Dermatology

CONTENTS

October 17, 1946

PAGE Section Volume

CASE FOR DIAGNOSIS. ? LICHEN PLANUS HYPERTROPHICUS
C. H. Whittle, M.D. 1 7

HÆMORRHAGIC TELANGIECTASIA OF RENDU-OSLER-WEBER, WITH NO FAMILY HISTORY
C. H. Whittle, M.D. 1 7

HÆMORRHAGIC TELANGIECTASIA OF RENDU-OSLER-WEBER
C. H. Whittle, M.D. 1 7

DARIER'S DISEASE AND GENERALIZED PRURITIS
Louis Forman, M.D. 2 8

CASE FOR DIAGNOSIS. ? LICHEN SCLEROSUS
H. J. Wallace, M.D. 2 8

KERATODERMA PALMARIS ET PLANTARUS
G. C. Wells, M.R.C.P. (for H. J. Wallace, M.D.) 3 9

LICHEN NITIDUS
J. R. Simpson, M.B. (for H. J. Wallace, M.D.) 3 9

EFFECT OF CALCIFEROL ON LUPUS VULGARIS (TWO CASES), LUPUS PERNIO AND BOECK'S SARCOID
I. R. Marre, L.R.C.P., M.R.C.S. 4 10

SARCOIDOSIS TREATED WITH CALCIFEROL
Brian Russell, M.D. 6 12

CASE FOR DIAGNOSIS. ? RETICULOSIS. ? CIRCUMSCRIBED MYXŒDEMA
Brian Russell, M.D. 6 12

MILIARY LYMPHOCYTOMA
F. R. Bettley, M.R.C.P... .. .. 7 13

DERMATITIS BULLOSA STRIATA PRATENSIS
H. Gruebel Lee, M.B., Ch.B. (introduced by Dr. I. Muende) 8 14

November 21, 1946

ULCER OF VULVA IN YOUNG GIRL
M. Moore White, M.D. (by kind permission and in conjunction with R. T. Brain, F.R.C.P.) 9 243

MULTIPLE TUBERCULIDES, INCLUDING THE SCLERODERMA-LIKE FORM OF ERYTHEMA INDURATUM
H. W. BARBER, M.B. 11 245

EXFOLIATIVE ERYTHRODERMIA WITH MARKED PIGMENTATION
J. E. M. Wigley, M.B. 12 246

IMPETIGO HERPETIFORMIS. ? PEMPHIGUS VEGETANS
J. E. M. Wigley, M.B. 14 248

PAPULO-NECROTIC TUBERCULIDES
Louis Forman, M.D. 14 248

LEIOMYOMA CUTIS
G. B. Mitchell-Heggs, O.B.E., F.R.C.P., and M. H. Small, M.R.C.S., L.R.C.P. 15 249

ERYTHRODERMIA IN LYMPHATIC LEUKÆMIA (MALIGNANT ERYTHRODERMIA)
G. B. Mitchell-Heggs, O.B.E., F.R.C.P., H. Corsi, F.R.C.S., and K. D. Crow, M.R.C.P. 15 249

? EPIDERMODYSPLASIA OF LEWANDOWSKI AND LUTZ. ? ABORTIVE FORM OF BLASTOMYCOSIS OR CHROMOBLASTOMYCOSIS
H. W. Allen, D.M. 17 251

A HEREDITARY ECTODERMAL DYSPLASIA, HITHERTO NOT DESCRIBED, INCLUDING GROUPED COMEDONES
C. H. Whittle, M.D. 17 251

? KAPOSI'S VARICELLIFORM ERUPTION
C. H. Whittle, M.D. 18 252

LUPUS VULGARIS AND TUBERCULIDES OF FACE
Bernard Green, M.R.C.S., L.R.C.P. 19 253

CUTANEOUS PAPILLOMATOSIS
R. M. B. MacKenna, M.D., and Brian Russell, M.D. 20 254

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF ENDOCRINOLOGY

OFFICERS:

President—L. R. BROSTER, O.B.E., M.Ch.

Vice-President—H. GARDINER-HILL, M.D.

Hon. Secretaries—RAYMOND GREENE, D.M.; P. M. F. BISHOP, D.M.

Other Members of Council—R. D. LAWRENCE, M.D.; A. S. PARKES, Ph.D., F.R.S.; E. F. SCOWEN, M.D.; S. L. SIMPSON, M.D.; A. W. SPENCE, M.D.

Representative on Library Committee—C. L. COPE, D.M.

Representative on Editorial Committee—A. C. CROOKE, M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7 CLIFFORD STREET, W.1.
1947

March 20, 1947

	PAGE Section	PAGE Volume
PARAPSORIASIS, RETIFORM VARIETY J. E. M. Wigley, F.R.C.P.	45	699
ACNE CONGLOBATA L. Forman, M.D.	45	699
PRINGLE'S DISEASE (ADENOMA SEBACEUM) Hugh W. Gordon, M.C., M.B.	46	700
MYCOSIS FUNGOIDES Hugh W. Gordon, M.C., M.B.	46	700
? ERYTHEMA MULTIFORME C. H. Whittle, M.D.	47	701
CONGENITAL ICHTHYOSIFORM ERYTHRODERMIA (BROCQ) Ian Martin Scott, M.D.	47	701
MYXŒDEMA PAPULOSUM Bernard Green, M.R.C.S., L.R.C.P., and W. Freudenthal, M.D.	48	702
SARCOIDOSIS Bernard Green, M.R.C.S., L.R.C.P., and C. W. F. McKean, M.B.	50	704
EPIDERMOLYSIS BULLOSA DYSTROPHICA C. W. F. McKean, M.B.	51	705
SENEAR-USHER SYNDROME E. Colin Jones, M.B.	51	705

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF ENDOCRINOLOGY

OFFICERS:

President—L. R. BROSTER, O.B.E., M.Ch.

Vice-President—H. GARDINER-HILL, M.D.

Hon. Secretaries—RAYMOND GREENE, D.M.; P. M. F. BISHOP, D.M.

Other Members of Council—R. D. LAWRENCE, M.D.; A. S. PARKES, Ph.D., F.R.S.; E. F. SCOWEN, M.D.; S. L. SIMPSON, M.D.; A. W. SPENCE, M.D.

Representative on Library Committee—C. L. COPE, D.M.

Representative on Editorial Committee—A. C. CROOKE, M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7 CLIFFORD STREET, W.1.
1947

March 20, 1947

	PAGE *Section*	*Volume*
PARAPSORIASIS, RETIFORM VARIETY J. E. M. Wigley, F.R.C.P.	45	699
ACNE CONGLOBATA L. Forman, M.D.	45	699
PRINGLE'S DISEASE (ADENOMA SEBACEUM) Hugh W. Gordon, M.C., M.B.	46	700
MYCOSIS FUNGOIDES Hugh W. Gordon, M.C., M.B.	46	700
? ERYTHEMA MULTIFORME C. H. Whittle, M.D.	47	701
CONGENITAL ICHTHYOSIFORM ERYTHRODERMIA (BROCQ) Ian Martin Scott, M.D.	47	701
MYXŒDEMA PAPULOSUM Bernard Green, M.R.C.S., L.R.C.P., and W. Freudenthal, M.D.	48	702
SARCOIDOSIS Bernard Green, M.R.C.S., L.R.C.P., and C. W. F. McKean, M.B.	50	704
EPIDERMOLYSIS BULLOSA DYSTROPHICA C. W. F. McKean, M.B.	51	705
SENEAR-USHER SYNDROME E. Colin Jones, M.B.	51	705

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF ENDOCRINOLOGY

OFFICERS:

President—L. R. BROSTER, O.B.E., M.Ch.

Vice-President—H. GARDINER-HILL, M.D.

Hon. Secretaries—RAYMOND GREENE, D.M.; P. M. F. BISHOP, D.M.

Other Members of Council—R. D. LAWRENCE, M.D.; A. S. PARKES, Ph.D., F.R.S.; E. F. SCOWEN, M.D.; S. L. SIMPSON, M.D.; A. W. SPENCE, M.D.

Representative on Library Committee—C. L. COPE, D.M.

Representative on Editorial Committee—A. C. CROOKE, M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7 CLIFFORD STREET, W.1.
1947

March 20, 1947

	PAGE *Section*	*Volume*
PARAPSORIASIS, RETIFORM VARIETY J. E. M. Wigley, F.R.C.P.	45	699
ACNE CONGLOBATA L. Forman, M.D.	45	699
PRINGLE'S DISEASE (ADENOMA SEBACEUM) Hugh W. Gordon, M.C., M.B.	46	700
MYCOSIS FUNGOIDES Hugh W. Gordon, M.C., M.B.	46	700
? ERYTHEMA MULTIFORME C. H. Whittle, M.D.	47	701
CONGENITAL ICHTHYOSIFORM ERYTHRODERMIA (BROCQ) Ian Martin Scott, M.D.	47	701
MYXŒDEMA PAPULOSUM Bernard Green, M.R.C.S., L.R.C.P., and W. Freudenthal, M.D.	48	702
SARCOIDOSIS Bernard Green, M.R.C.S., L.R.C.P., and C. W. F. McKean, M.B.	50	704
EPIDERMOLYSIS BULLOSA DYSTROPHICA C. W. F. McKean, M.B.	51	705
SENEAR-USHER SYNDROME E. Colin Jones, M.B.	51	705

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

Edited Under the Direction of the EDITORIAL COMMITTEE
Honorary Editors: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF EPIDEMIOLOGY AND STATE MEDICINE

OFFICERS:

President—H. J. Parish, M.D.

Vice-Presidents—J. A. H. Brincker, M.B.; William Butler, M.B.; S. Monckton Copeman, M.D., F.R.S.; Sir Weldon Dalrymple-Champneys, Bt., F.R.C.P.; Surgeon Vice-Admiral Sir Sheldon Dudley, K.C.B., F.R.S.; J. Alison Glover, C.B.E., M.D.; E. H. R. Harries, M.D.; Sir Arthur MacNalty, K.C.B., M.D.; P. G. Stock, C.B., F.R.C.P.

Hon. Secretaries—E. Ashworth Underwood, M.D.; W. H. Bradley, D.M.

Hon. Secretary for Navy—Surg. Capt. R. W. Mussen, R.N.

Hon. Secretary for Army—Brigadier J. S. K. Boyd, O.B.E.

Hon. Secretary for R.A.F.—Air Commodore T. McClurkin.

Dominion and Foreign Hon. Secretaries—Robert C. Pierret, M.D. (France); N. Hamilton Fairley, O.B.E., F.R.C.P., F.R.S. (Australia); P. G. Stock, C.B., F.R.C.P. (South Africa); Surg. General Hugh S. Cumming (U.S.A.).

Other Members of Council—V. D. Allison, M.D.; J. L. Burn, M.D.; W. S. C. Copeman, O.B.E., F.R.C.P.; Sir Allen Daley, M.D.; W. Gunn, F.R.C.P.; A. Bradford Hill, Ph.D.; Sir Wilson Jameson, K.C.B., M.D.; J. E. McCartney, M.D.; Allan McFarlan, M.B.; James M. Mackintosh, M.D.; Melville Mackenzie, C.M.G., M.D.; R. A. O'Brien, C.B.E., M.D.; C. O. Stallybrass, M.D.; Percy Stocks, M.D.; G. Clark Trotter, M.D.

Representative on Library Committee—E. Ashworth Underwood, M.D.

Representative on Editorial Committee—Allan McFarlan, M.B.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W 1
1947

Section of Endocrinology

CONTENTS

October 23, 1946

	PAGE Section	PAGE Volume
DISCUSSION: OVERACTIVITY OF THE ADRENAL CORTEX	1–12	35–46
Mr. L. R. Broster	1	35
Dr. E. F. Scowen and Dr. F. L. Warren	5	39
Dr. A. C. Crooke	9	43
Dr. A. S. Parkes, Dr. S. L. Simpson	11	45
Dr. J. Patterson, Dr. R. K. Callow	12	46

November 29, 1946

	PAGE Section	PAGE Volume
CHROMOPHOBE ADENOMA IN A MALE AGED 15½ YEARS S. Leonard Simpson, M.D., and A. Dickson Wright, M.S.	13	151
CHROMOPHOBE ADENOMA IN A MALE AGED 67 YEARS S. Leonard Simpson, M.D., and Julian Taylor, O.B.E., M.S.	13	151
PITUITARY INFANTILISM WITH TOXIC GOITRE A. W. Spence, M.D.	13	151
LONG-STANDING HYPOPITUITARISM WITH RECENT SIGNS SUGGESTING EITHER CHROMOPHILIC ADENOMA OR SUPRASELLAR TUMOUR H. S. Le Marquand, M.D.	14	152
PAN-HYPOPITUITARISM R. S. Bruce Pearson, D.M.	15	153
CASE FOR DIAGNOSIS. ? DIABETES MELLITUS WITH DIABETES INSIPIDUS A. C. Crooke, M.D.	15	153
BASOPHILISM TREATED UNSUCCESSFULLY WITH MASSIVE DOSES OF ŒSTROGENS AND DEEP X-RAY THERAPY, BUT CURED BY RADON SEEDS INSERTED INTO THE SELLA TURCICA A. C. Crooke, M.D.	15	153
PRIMARY HYPERPLASIA OF THE PARATHYROIDS IN A BOY AGED 8 YEARS N. F. Elliott Burrows, B.M. (for W. G. Wyllie, F.R.C.P.)	16	154
PRECOCIOUS PUBERTY OF ? SUPRARENAL ORIGIN N. F. Elliott Burrows, B.M. (for W. G. Wyllie, F.R.C.P.)	16	154

March 26, 1947

	PAGE Section	PAGE Volume
DISCUSSION ON THE TREATMENT OF TOXIC GOITRE	17–24	609–616
Mr. J. E. Piercy	17	609
Dr. W. R. Trotter	18	610
Dr. A. M. Nussey	22	614
Mr. R. Vaughan Hudson	23	615
Dr. A. C. Crooke	24	616

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF EXPERIMENTAL MEDICINE AND THERAPEUTICS

OFFICERS:

President—H. P. HIMSWORTH, M.D.

Immediate Past-President—E. N. ALLOTT, F.R.C.P.

Vice-Presidents—R. V. CHRISTIE, M.D.; R. D. LAWRENCE, M.D.; R. A. MCCANCE, M.D.; JANET VAUGHAN, O.B.E., D.M.

Hon. Secretaries—W. G. OAKLEY, M.D.; K. M. A. PERRY, M.D.

Other Members of Council—F. AVERY JONES, M.D.; J. F. LOUTIT, M.R.C.P.; R. G. MACFARLANE, M.D.; J. MCMICHAEL, M.D.; G. W. PICKERING, F.R.C.P.; J. F. WILKINSON, M.D.; CLIFFORD WILSON, D.M.

Representative on Library Committee—W. W. PAYNE, M.B.

Representative on Editorial Committee—A. C. WHITE, M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Epidemiology and State Medicine

CONTENTS

PAGE
Section *Volume*

October 25, 1946

DISCUSSION ON HEALTH PROBLEMS IN GERMANY 1–12 89–100
Colonel T. F. Kennedy 1 89
Dr. P. G. Horsburgh 5 93
Dr. H. A. Raeburn 9 97

November 22, 1946

DISCUSSION: MODERN METHODS IN THE CONTROL OF AIR-BORNE INFECTIONS. [*Abridged*] 13–15 381–383
Dr. R. Cruickshank 13 381
Dr. Joyce Wright, Mr. F. Courtney Harwood, Dr. O. M. Lidwell.. .. 14 382
Dr. M. Mitman, Major A. C. Cunliffe, Dr. J. L. Burn, Dr. J. M. Alston, Dr. William Gunn, Professor Ronald Hare 15 383

January 24, 1947

WHOOPING COUGH AND MEASLES. AN EPIDEMIOLOGICAL CONCURRENCE AND CONTRAST
William Butler, M.B. 16 384

February 28, 1947

DISCUSSION ON THE PRESENT STATUS OF INFECTIOUS DISEASE CONTROL IN CONTINENTAL EUROPE 31–40 623–632
Dr. Ian Taylor 31 623
Dr. H. Stanley Banks 35 627
Dr. F. R. Curtis 38 630
Dr. J. Balfour Kirk 39 631
Dr. Milosh Sekulich 40 632

May 2, 1947

COMMON COLD. INTERIM REPORT ON A TRANSMISSION EXPERIMENT. [*Abstract*]
Doctors C. H. Andrewes, W. H. Bradley, D. K. M. Chalmers and F. Fulton 40 632

March 28, 1947

MALARIA CONTROL WITH D.D.T. ON A NATIONAL SCALE—GREECE, 1946. [*Abridged*]
J. M. Vine, M.B., B.S.Melb., D.P.H.Eng. 43 841

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF EXPERIMENTAL MEDICINE AND THERAPEUTICS

OFFICERS:

President—H. P. HIMSWORTH, M.D.

Immediate Past-President—E. N. ALLOTT, F.R.C.P.

Vice-Presidents—R. V. CHRISTIE, M.D.; R. D. LAWRENCE, M.D.; R. A. MCCANCE, M.D.; JANET VAUGHAN, O.B.E., D.M.

Hon. Secretaries—W. G. OAKLEY, M.D.; K. M. A. PERRY, M.D.

Other Members of Council—F. AVERY JONES, M.D.; J. F. LOUTIT, M.R.C.P.; R. G. MACFARLANE, M.D.; J. MCMICHAEL, M.D.; G. W. PICKERING, F.R.C.P.; J. F. WILKINSON, M.D.; CLIFFORD WILSON, D.M.

Representative on Library Committee—W. W. PAYNE, M.B.

Representative on Editorial Committee—A. C. WHITE, M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Experimental Medicine and Therapeutics

CONTENTS

	PAGE Section	PAGE Volume
October 8, 1946		
PROTEIN METABOLISM IN RELATION TO DISEASE President's Address by Professor H. P. Himsworth, M.D.	1	27
January 14, 1947		
NUTRITIONAL LIVER DISEASE IN WEST INDIAN INFANTS J. C. Waterlow, M.B.	9	347
SOME RENAL EFFECTS OF EXPERIMENTAL DIETARY DEFICIENCIES H. Heller, M.B., Ph.D., and S. E. Dicker, M.D.	13	351
February 11, 1947		
DISCUSSION ON RADIOACTIVE TRACERS	16–22	354–360
Dr. A. S. McFarlane	16	354
Dr. E. E. Pochin	19	357
Professor A. St.G. Huggett, Dr. McFarlane, Professor H. P. Himsworth	22	360
July 17, 1947		
Joint Meeting with the Medical Society for the Study of Venereal Diseases.		
DISCUSSION ON THE TREATMENT OF SYPHILIS WITH PENICILLIN	23–28	811–816
Dr. Joseph Earle Moore, U.S.A.	23	811
Dr. E. M. Lourie	26	814
Lieut.-Colonel J. W. Eames, R.A.M.C., Mr. A. J. King	27	815
Dr. R. Forgan, Dr. David Nabarro, Dr. J. Earle Moore	28	816

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Edited Under the Direction of the EDITORIAL COMMITTEE

Honorary Editors: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF THE HISTORY OF MEDICINE

OFFICERS:

President—Sir Arthur MacNalty, K.C.B., M.D.

Vice-Presidents—S. Lyle Cummins, C.B., M.D.; S. H. Daukes, O.B.E., M.D.; J. Alison Glover, C.B.E., M.D.; Charles Singer, M.D.; Mrs. Dorothea Singer.

Honorary Secretaries—H. J. Norman, M.B.; E. Ashworth Underwood, M.D.

Other Members of Council—H. P. Bayon, M.D.; W. R. Bett; A. P. Cawadias, O.B.E., M.D.; A. E. Evans, M.B.; Douglas Guthrie, M.D.; Mrs. Lilian Lindsay, C.B.E.; R. O. Moon, M.D.; J. A. Nixon, C.M.G., M.D.; A. H. T. Robb-Smith, M.D.; J. H. Harley Williams, M.D.

Representative on Library Committee—A. P. Cawadias, O.B.E., M.D.

Representative on Editorial Committee—A. P. Cawadias, O.B.E., M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of the History of Medicine

CONTENTS

PAGE
Section Volume

October 2, 1946

THE EVOLUTION OF PREVENTIVE MEDICINE IN ENGLAND
President's Address by Sir Arthur Salusbury MacNalty, K.C.B., M.A., M.D., F.R.C.P. .. 1 59

October 16, 1946

THE DEVELOPMENT OF INHALATION ANÆSTHESIA IN THE SECOND HALF OF THE NINETEENTH CENTURY
Barbara Duncum, Ph.D. .. 10 68

January 8, 1947

CLINICAL SCIENCE IN THE LIGHT OF HISTORY
A. P. Cawadias, O.B.E., M.D., F.R.C.P. .. 17 453

May 8, 1947

THE PRE-HISTORY OF MIDWIFERY [*Abridged*]
I. Harvey Flack, M.D. .. 27 713

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.

ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF LARYNGOLOGY

OFFICERS:

President—NORMAN PATTERSON, F.R.C.S.

Immediate Past-President—G. EWART MARTIN, F.R.C.S.Ed.

Past-Presidents—W. M. MOLLISON, C.B.E., M.Ch.; E. D. D. DAVIS, F.R.C.S.

Vice-Presidents—W. I. DAGGETT, F.R.C.S.; DONALD WATSON, F.R.C.S.; E. MUSGRAVE WOODMAN, M.S.

Hon. Secretaries—G. H. BATEMAN, F.R.C.S.; J. E. G. MCGIBBON, O.B.E., M.B.

Other Members of Council—W. H. BRADBEER, M.S.; MYLES FORMBY, F.R.C.S.; R. G. MACBETH, F.R.C.S.Ed.; ROYDON PEACOCK, F.R.C.S.; IAN G. ROBIN, F.R.C.S.; W. L. THOMAS, F.R.C.S.; A. S. H. WALFORD, F.R.C.S.; GAVIN YOUNG, M.B.

Representative on Library Committee—V. E. NEGUS, M.S.

Representative on Editorial Committee—LIONEL COLLEDGE, F.R.C.S.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Laryngology

CONTENTS

PAGE
Section Volume

December 6, 1946

EMERGENCY EPISTAXIS
Josephine Collier .. 1 277
ANTERIOR ETHMOIDAL HÆMORRHAGE
R. G. Macbeth .. 4 280
CHOANAL ATRESIA
T. M. Boyle .. 7 283
PEMPHIGUS OF PHARYNX
H. S. Sharp .. 8 284
GUMMATOUS DESTRUCTION OF NASAL SEPTUM: PERFORATING EPITHELIOMA OF NOSE
H. S. Sharp .. 8 284
AN AID TO SWALLOWING AFTER LARYNGO-PHARYNGECTOMY FOR POST-CRICOID CARCINOMA
H. A. Kidd .. 8 284
RECURRENT CHONDROMA OF THE SUBGLOTTIC REGION
F. C. W. Capps .. 9 285
PERSISTENT EPIPHORA FOLLOWING ACUTE DACRYOCYSTITIS
Brian Reeves .. 9 285
RECURRENT PAPILLOMATA AND WEBBING OF THE LARYNX
D. F. A. Neilson .. 10 286
CONGENITAL BILATERAL FISTULA OF TEAR DUCT, ONE SIDE TREATED BY TOTI'S OPERATION
J. F. Simpson .. 10 286
OSTEOMA OF NASOPHARYNX
A. W. McCay .. 10 286
PRELIMINARY MODEL FOR AN INDIRECT LARYNGOSCOPE
W. O. Lodge .. 10 286

February 7, 1947

INTRINSIC CANCER OF THE LARYNX, REVIEW OF A SERIES OF CASES
V. E. Negus .. *11* *515*
B. W. Windeyer .. 18 522

March 7, 1947

THE DIAGNOSIS AND TREATMENT OF TUMOURS OF THE NASOPHARYNX
E. D. D. Davis .. 21 707

SECTION OF LARYNGOLOGY WITH SECTION OF OTOLOGY
COMBINED SUMMER MEETING HELD IN BRIGHTON
LARYNGOLOGICAL SESSION

June 27, 1947

CERTAIN ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS IN PARALYSIS OF THE LARYNX
V. E. Negus .. 27 849
THE TREATMENT OF SUBACUTE MAXILLARY SINUSITIS ESPECIALLY IN CHILDREN
G. E. Archer .. 32 854
FILM: "BRONCHIAL NEOPLASMS"
Paul H. Holinger, Chicago (shown by G. H. Bateman) .. 36 858

(For Otological Session *see* Vol. 41, p. 1.)

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF MEDICINE

OFFICERS:

President—MAURICE DAVIDSON, M.D.

Vice-Presidents—Sir JOHN J. CONYBEARE, K.B.E., F.R.C.P.; E. R. CULLINAN, M.D.; GEOFFREY EVANS, M.D.; H. GARDINER-HILL, M.D.; J. L. LIVINGSTONE, M.D.; C. E. NEWMAN, M.D.; G. W. PICKERING, F.R.C.P.; Sir ALUN ROWLANDS, K.B.E., F.R.C.P.; Sir ARNOLD STOTT, K.B.E., F.R.C.P.; Sir HENRY TIDY, K.B.E., M.D.

Hon. Secretaries—A. MORTON GILL, M.D.; R. BODLEY SCOTT, F.R.C.P.

Other Members of Council—GEOFFREY BOURNE, M.D.; P. E. THOMPSON HANCOCK, F.R.C.P.; JAMES MAXWELL, M.D.; R. S. BRUCE PEARSON, D.M.; N. S. PLUMMER, F.R.C.P.; A. W. SPENCE, M.D.; E. C. WARNER, M.D.

Representative on Library Committee—REGINALD HILTON, F.R.C.P.

Representative on Editorial Committee—MAURICE DAVIDSON, M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Medicine

CONTENTS

November 26, 1946

	PAGE Section	PAGE Volume
DISCUSSION ON BIRTH CONTROL: SOME MEDICAL AND LEGAL ASPECTS	1–8	51–58
Dr. Maurice Davidson, Dr. E. B. Ford	1	51
Mr. Aleck Bourne	2	52
Dr. Kenneth McFadyean	5	55
Sir Travers Humphreys, Mr. Reynold Boyd, Mr. V. B. Green-Armytage, Mr. Anthony W. Purdie	7	57
Dr. Letitia Fairfield, Dr. Alexander Kennedy, Dr. Edward F. Griffith	8	58
ADDENDUM: Dr. Eustace Chesser	—	346

February 25, 1947

DISCUSSION: TREATMENT OF THE LYMPHADENOPATHIES	9–14	617–622
Dr. R. Bodley Scott	9	617
Professor M. J. Stewart, Dr. E. Lipman Cohen, Professor D. W. Smithers	13	621
Dr. J. D. N. Nabarro	14	622

March 25, 1947

PAINFUL DISABILITY OF THE SHOULDER IN CORONARY DISEASE A. Schott, M.D.	15	733
COLLAPSE OF THE LOWER LOBES OF THE LUNGS IN CHILDREN Neville C. Oswald, M.D., F.R.C.P.	18	736
OSTEOMALACIA [*Summary*] J. Preston Maxwell, M.D., F.R.C.S., F.R.C.O.G.	20	738

April 22, 1947

DISCUSSION: THE MANAGEMENT OF PATIENTS WITH ESSENTIAL HYPERTENSION	23–30	773–780
Dr. Geoffrey Evans	23	773
Mr. A. Dickson Wright	24	774
Dr. C. H. Wyndham	26	776
Mr. H. J. B. Atkins	28	778
Dr. Evan Bedford	29	779
Dr. T. H. Whittington, Mr. A. Dickson Wright	30	780

May 27, 1947

DISCUSSION: THE PRESENT POSITION IN REGARD TO THE PNEUMOCONIOSES	31–36	781–786
Dr. E. R. A. Merewether	31	781
Dr. C. M. Fletcher, Professor Matthew J. Stewart	33	783

SECTION OF MEDICINE WITH SECTION OF PHYSICAL MEDICINE
(*JOINT DISCUSSION No.* 1)

January 28, 1947

THE ÆTIOLOGY OF CHRONIC RHEUMATISM	—	329–346
Dr. W. S. C. Copeman	—	329
Dr. Philip Ellman	—	332
Dr. G. D. Kersley	—	343
Dr. Ernest Fletcher, Dr. W. R. Thrower, Dr. W. Annandale Troup	—	345
Dr. W. Ganado	—	346

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Edited Under the Direction of the EDITORIAL COMMITTEE
Honorary Editors: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF NEUROLOGY

OFFICERS:

President—Douglas McAlpine, M.D.

Vice-Presidents—William Johnson, M.C., M.D.; C. Worster-Drought, M.D.

Hon. Secretaries—Wylie McKissock, O.B.E., M.S.; J. St. C. Elkington, M.D.

Other Members of Council—Denis Brinton, F.R.C.P.; Sir Hugh Cairns, K.B.E., F.R.C.S.; Colin Edwards, M.R.C.P.; S. P. Meadows, M.D.; F. J. Nattrass, M.D.; J. Purdon Martin, M.D.; J. E. A. O'Connell, F.R.C.S.; Andrew Paterson, M.D.; Joe Pennybacker, F.R.C.S.; Eliot Slater, M.D.; Sir Charles P. Symonds, K.B.E., M.D.

Representative on Library Committee—G. C. Knight, F.R.C.S.

Representative on Editorial Committee—Wylie McKissock, O.B.E., M.S.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Neurology

CONTENTS

November 7, 1946

MEETING AT THE MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, W.9

	PAGE Section	PAGE Volume
ATAXIC NYSTAGMUS IN DISSEMINATED SCLEROSIS Wilfred Harris, M.D., F.R.C.P.	1	81
TUBEROSE SCLEROSIS WITH INTRACRANIAL CALCIFICATION AND LESIONS OF BONE Helen Dimsdale, M.R.C.P.	1	81
GLOSSOPHARYNGEAL NEURALGIA TREATED BY TRANS-TONSILLAR SECTION OF THE NERVE C. P. Wilson, C.V.O., F.R.C.S., and D. McAlpine, M.D., F.R.C.P. ..	2	82
COMPRESSION NEURITIS OF BOTH MEDIAN NERVES IN THE CARPAL TUNNEL: SURGICAL DECOMPRESSION. KLIPPEL-FEIL DEFORMITY OF NECK. SPRENGEL SHOULDER W. Russell Brain, D.M., and A. Dickson Wright, M.S.	3	83
TEMPORAL ARTERITIS Michael Kremer, M.D., F.R.C.P.	4	84
PAGET'S DISEASE OF THE SKULL WITH PLATYBASIA James Bull, M.B., M.R.C.P.	5	85
AFFECTION OF THE TRIGEMINAL NERVE NUCLEUS AND CENTRAL GREY MATTER OF THE SPINAL CORD FOLLOWING THE ADMINISTRATION OF STILBAMIDINE Major P. Collard, R.A.M.C., and Professor S. Nevin, M.D.	7	87

December 12, 1946

DISCUSSION ON THE TREATMENT AND PROGNOSIS OF TRAUMATIC PARAPLEGIA	9–22	219–232
Dr. L. Guttmann	9	219
Mr. E. W. Riches	15	225
Dr. D. Whitteridge	19	229
Dr. P. H. A. Jonason	20	230
Dr. W. Ritchie Russell	21	231
Dr. P. W. Nathan, Dr. Giles Romanes, Mr. Riches, The President ..	22	232

February 6, 1947

CLINICAL MEETING HELD AT NATIONAL HOSPITAL, QUEEN SQUARE, LONDON

DYSTONIA MUSCULORUM DEFORMANS WITH ANOTHER CASE IN THE SAME FAMILY Diana Beck, F.R.C.S.	23	551
POST-ENCEPHALITIC PARKINSONISM WITH MARKED PALILALIA Macdonald Critchley, M.D.	24	552
PARAPLEGIC EUNUCH WITH LUES Macdonald Critchley, M.D.	24	552
MYOCLONUS E. A. Carmichael, C.B.E., M.B.	25	553
SPONTANEOUS CAROTID-CAVERNOUS ANEURYSM S. P. Meadows, M.D.	26	554
PAPILLŒDEMA ASSOCIATED WITH CHRONIC BRONCHITIS, EMPHYSEMA AND POLYCYTHÆMIA S. P. Meadows, M.D.	27	555
POLIOMYELITIS LIMITED TO BOTH TRIGEMINAL MOTOR NUCLEI Denis Williams, M.D.	27	555
WILSON'S DISEASE Denis Brinton, D.M.	28	556

Joint Meeting with the Société de Neurologie de Paris on April 15 and 17, 1947

April 15, 1947

	PAGE *Section*	 *Volume*
DISCUSSION ON PENICILLIN IN NEUROLOGY	29–34	681–686
Sir Hugh Cairns, Dr. Honor V. Smith	29	681
Dr. C. Worster-Drought	31	683
Dr. W. D. Nicol and Dr. M. Whelen	32	684

April 17, 1947

DISCUSSION ON CEREBRAL ŒDEMA	34–46	686–698
Professor Th. Alajouanine	34	686
Dr. Douglas McAlpine	36	688
Doctors Clovis Vincent, Jacques Le Beau et Gerard Guiot	37	689
Professor Geoffrey Jefferson	42	694
Dr. J. G. Greenfield	43	695
Dr. A. M. Stewart-Wallace	45	697

May 1, 1947

THE NORMAL TEMPORAL HORN AND ITS DEFORMITIES BY TUMOURS IN THE MIDDLE CEREBRAL FOSSA. [*Abstract*]		
Erik Lindgren, M.D.	47	859

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various]papers.

Printed by
STAPLES PRESS LIMITED
at their
Great Titchfield Street, London, establishment

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF OBSTETRICS & GYNÆCOLOGY

OFFICERS:

President—JAMES WYATT, F.R.C.S.

Past-Presidents—Sir GEORGE BLACKER, C.B.E., M.D.; W. GILLIATT, C.V.O., M.S.; J. MUNRO KERR, M.D.; MILES PHILLIPS, M.D.; Sir WILLIAM FLETCHER SHAW, M.D.; T. G. STEVENS, F.R.C.S.; F. J. BROWNE, M.D.

Vice-Presidents—ALECK BOURNE, F.R.C.S.; R. A. BREWS, F.R.C.S.; MALCOLM DONALDSON, F.R.C.S.; VICTOR LACK, F.R.C.S.Ed.; Dame LOUISE McILROY, D.B.E., M.D.; DOUGLAS MACLEOD, M.S.; PERCY MALPAS, F.R.C.S.; J. CHASSAR MOIR, F.R.C.S.Ed.; CHARLES READ, F.R.C.S.Ed.

Hon. Secretaries—W. R. WINTERTON, F.R.C.S.; A. J. WRIGLEY, M.D.

Other Members of Council—JOSEPHINE BARNES, D.M.; A. M. CLAYE, F.R.C.S.; GERTRUDE DEARNLEY, M.D.; GLADYS DODDS, F.R.C.S.; FRANK COOK, F.R.C.S.; J. D. S. FLEW, M.D.; J. P. HEDLEY, M.Ch.; GLADYS HILL, F.R.C.S.; MEAVE KENNY, M.B.; S. GORDON LUKER, F.R.C.S.; KATHLEEN ROBINSON, F.R.C.S.; F. W. ROQUES, M.Ch.; JOHN STALLWORTHY, F.R.C.S.; G. I. STRACHAN, M.Ch.; C. KEITH VARTAN, F.R.C.S.; NORMAN WHITE, F.R.C.S.; LESLIE WILLIAMS, M.S.; JAMES YOUNG, D.S.O., M.D.

Representative on Library Committee—C. M. GWILLIM, F.R.C.S.

Representative on Editorial Committee—L. CARNAC RIVETT, M.Ch.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Printed by
STAPLES PRESS LIMITED
at their
Great Titchfield Street, London, establishment

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Edited Under the Direction of the EDITORIAL COMMITTEE
Honorary Editors: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF ODONTOLOGY

OFFICERS:

President—H. Stobie, F.R.C.S., L.D.S.E.

Immediate Past-President—Lilian Lindsay, C.B.E., M.D.S.Durham, L.D.S.Ed.

Vice-Presidents—(Resident) Herbert Smale, L.R.C.P., M.R.C.S., L.D.S.E.; F. Bocquet Bull, L.R.C.P., M.R.C.S., L.D.S.E.; E. Wilfred Fish, C.B.E., M.D., L.D.S.Manch.; (Non-Resident) G. F. Fawn, L.R.C.P., M.R.C.S., L.D.S.E.; Colonel L. A. Harwood, L.R.C.P., M.R.C.S., L.D.S.E.; Ivan Spain, L.D.S.E.

Hon. Secretaries—A. B. MacGregor, M.D., L.D.S.E.; D. Greer Walker, M.B., M.Dent.Sc.Dublin.

Hon. Curator—Sir Frank Colyer, K.B.E., F.R.C.S., L.D.S.E.

Hon. Secretary for Foreign Correspondence—Martin A. Rushton, M.D., L.D.S.E.

Other Members of Council—(Resident) B. Maxwell Stephens, L.D.S.E.; Harold Chapman, L.D.S.E.; W. Kelsey Fry, M.C., L.R.C.P., M.R.C.S., L.D.S.E.; R. E. Rix, L.R.C.P., M.R.C.S., L.D.S.E.; A. Bulleid, L.R.C.P., M.R.C.S., L.D.S.E.; H. L. Hardwick, L.D.S.E.; W. E. Herbert, L.R.C.P., M.R.C.S., L.D.S.E.; H. H. Kenshole, D.S.O., L.R.C.P., M.R.C.S., L.D.S.E.; H. A. Mahoney, L.D.S. R.C.S.Ed.; (Non-resident) B. W. Fickling, F.R.C.S., L.D.S.E.; E. B. Manley, B.D.S.Birm.; C. W. Nicholas, L.D.S.Glas.; G. C. Friend, L.D.S.Bristol; Martin A. Rushton, M.D., L.D.S.E.; Humphrey Humphreys, O.B.E., M.B., Ch.B., L.D.S.E.; H. Slater, L.D.S.E.; P. J. Stoy, L.D.S.E., B.D.S.Birm.; Keith R. Titford, B.D.S.Lond., L.D.S.E.

Representative on Library Committee—G. T. Hankey, O.B.E., L.R.C.P., M.R.C.S., L.D.S.E.

Representative on Editorial Committee—B. W. Fickling, F.R.C.S., L.D.S.E.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Obstetrics & Gynæcology

CONTENTS

PAGE
Section Volume

November 15, 1946

DISCUSSION ON STRESS INCONTINENCE IN MICTURITION .. 1–10 361–370
Mr. Everard Williams .. 1 361
Mr. Terence Millin .. 4 364
Professor J. Chassar Moir .. 7 367
Mr. D. M. Stern .. 10 370

January 17, 1947

DISCUSSION ON THE MANAGEMENT OF THE NORMAL THIRD STAGE OF LABOUR AND OF HÆMORRHAGE THEREIN .. 10–16 370–376
Mr. J. D. S. Flew .. 10 370
Professor Hilda N. Lloyd .. 11 371
Dr. Peter Denham .. 13 373
Mr. G. F. Gibberd .. 15 375

February 21, 1947

THE TREATMENT OF TUBERCULOUS SALPINGITIS WITH SPECIAL REFERENCE TO X-RAY THERAPY
Elliot Philipp, M.R.C.S., L.R.C.P. .. 16 376
FULL-TERM INTRALIGAMENTARY PREGNANCY
I. T. Fraser, F.R.C.S.Ed. .. 18 378
UTERINE RUPTURE
Ian Donald, M.B. .. 19 379

March 21, 1947

DISCUSSION ON ANÆSTHESIA FOR CÆSAREAN SECTION .. 21–32 557–568
Mr. Rufus C. Thomas .. 21 557
Mr. J. H. Peel .. 23 559
Mr. C. McIntosh Marshall .. 24 560
Dr. Katherine Lloyd-Williams .. 26 562
Dr. C. J. Massey Dawkins .. 28 564
Dr. J. N. Cave .. 30 566
Mr. Linton Snaith .. 31 567
Mr. H. J. Malkin, Dr. J. B. Cochrane .. 32 568

June 20, 1947

DISCUSSION ON SOME RECENT DEVELOPMENTS IN KNOWLEDGE OF THE PHYSIOLOGY OF THE BREAST .. 33–40 899–906
Dr. S. Engel .. 33 899
Dr. S. K. Kon and Dr. Elinor Huntsman Mawson .. 34 900
Dr. S. J. Folley .. 37 903

SECTION OF OBSTETRICS AND GYNÆCOLOGY WITH SECTION OF RADIOLOGY

(*JOINT DISCUSSION No.* 3)

May 16, 1947

DISCUSSION ON SOME ASPECTS OF SURGICAL AND RADIOLOGICAL TREATMENT OF CARCINOMA OF THE CERVIX .. — 907–922
Professor Subodh Mitra, F.R.C.S.Ed., F.R.C.O.G.(Calcutta) .. — 907
Mr. Charles D. Read .. — 909
G. E. Richards, M.D. (Toronto)* .. — 911
Mr. G. W. Blomfield .. — 917
Mr. Frank Cook .. — 922

* *See also* Vol. 41, p. 150.

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF ODONTOLOGY

OFFICERS:

President—H. STOBIE, F.R.C.S., L.D.S.E.

Immediate Past-President—LILIAN LINDSAY, C.B.E., M.D.S.Durham, L.D.S.Ed.

Vice-Presidents—(Resident) HERBERT SMALE, L.R.C.P., M.R.C.S., L.D.S.E.; F. BOCQUET BULL, L.R.C.P., M.R.C.S., L.D.S.E.; E. WILFRED FISH, C.B.E., M.D., L.D.S.Manch.; (Non-Resident) G. F. FAWN, L.R.C.P., M.R.C.S., L.D.S.E.; Colonel L. A. HARWOOD, L.R.C.P., M.R.C.S., L.D.S.E.; IVAN SPAIN, L.D.S.E.

Hon. Secretaries—A. B. MACGREGOR, M.D., L.D.S.E.; D. GREER WALKER, M.B., M.Dent.Sc.Dublin.

Hon. Curator—Sir FRANK COLYER, K.B.E., F.R.C.S., L.D.S.E.

Hon. Secretary for Foreign Correspondence—MARTIN A. RUSHTON, M.D., L.D.S.E.

Other Members of Council—(Resident) B. MAXWELL STEPHENS, L.D.S.E.; HAROLD CHAPMAN, L.D.S.E.; W. KELSEY FRY, M.C., L.R.C.P., M.R.C.S., L.D.S.E.; R. E. RIX, L.R.C.P., M.R.C.S., L.D.S.E.; A. BULLEID, L.R.C.P., M.R.C.S., L.D.S.E.; H. L. HARDWICK, L.D.S.E.; W. E. HERBERT, L.R.C.P., M.R.C.S., L.D.S.E.; H. H. KENSHOLE, D.S.O., L.R.C.P., M.R.C.S., L.D.S.E.; H. A. MAHONEY, L.D.S. R.C.S.Ed.; (Non-resident) B. W. FICKLING, F.R.C.S., L.D.S.E.; E. B. MANLEY, B.D.S.Birm.; C. W. NICHOLAS, L.D.S.Glas.; G. C. FRIEND, L.D.S.Bristol; Martin A. RUSHTON, M.D., L.D.S.E.; HUMPHREY HUMPHREYS, O.B.E., M.B., Ch.B., L.D.S.E.; H. SLATER, L.D.S.E.; P. J. STOY, L.D.S.E., B.D.S.Birm.; Keith R. TITFORD, B.D.S.Lond., L.D.S.E.

Representative on Library Committee—G. T. HANKEY, O.B.E., L.R.C.P., M.R.C.S., L.D.S.E.

Representative on Editorial Committee—B. W. FICKLING, F.R.C.S., L.D.S.E.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Obstetrics & Gynæcology

CONTENTS

November 15, 1946

	PAGE Section	PAGE Volume
DISCUSSION ON STRESS INCONTINENCE IN MICTURITION	1–10	361–370
Mr. Everard Williams	1	361
Mr. Terence Millin	4	364
Professor J. Chassar Moir	7	367
Mr. D. M. Stern	10	370

January 17, 1947

	Section	Volume
DISCUSSION ON THE MANAGEMENT OF THE NORMAL THIRD STAGE OF LABOUR AND OF HÆMORRHAGE THEREIN	10–16	370–376
Mr. J. D. S. Flew	10	370
Professor Hilda N. Lloyd	11	371
Dr. Peter Denham	13	373
Mr. G. F. Gibberd	15	375

February 21, 1947

	Section	Volume
THE TREATMENT OF TUBERCULOUS SALPINGITIS WITH SPECIAL REFERENCE TO X-RAY THERAPY		
Elliot Philipp, M.R.C.S., L.R.C.P.	16	376
Full-term Intraligamentary Pregnancy		
I. T. Fraser, F.R.C.S.Ed.	18	378
Uterine Rupture		
Ian Donald, M.B.	19	379

March 21, 1947

	Section	Volume
DISCUSSION ON ANÆSTHESIA FOR CÆSAREAN SECTION	21–32	557–568
Mr. Rufus C. Thomas	21	557
Mr. J. H. Peel	23	559
Mr. C. McIntosh Marshall	24	560
Dr. Katherine Lloyd-Williams	26	562
Dr. C. J. Massey Dawkins	28	564
Dr. J. N. Cave	30	566
Mr. Linton Snaith	31	567
Mr. H. J. Malkin, Dr. J. B. Cochrane	32	568

June 20, 1947

	Section	Volume
DISCUSSION ON SOME RECENT DEVELOPMENTS IN KNOWLEDGE OF THE PHYSIOLOGY OF THE BREAST	33–40	899–906
Dr. S. Engel	33	899
Dr. S. K. Kon and Dr. Elinor Huntsman Mawson	34	900
Dr. S. J. Folley	37	903

SECTION OF OBSTETRICS AND GYNÆCOLOGY WITH SECTION OF RADIOLOGY

(*JOINT DISCUSSION No.* 3)

May 16, 1947

	Section	Volume
DISCUSSION ON SOME ASPECTS OF SURGICAL AND RADIOLOGICAL TREATMENT OF CARCINOMA OF THE CERVIX	—	907–922
Professor Subodh Mitra, F.R.C.S.Ed., F.R.C.O.G.(Calcutta)	—	907
Mr. Charles D. Read	—	909
G. E. Richards, M.D. (Toronto)*	—	911
Mr. G. W. Blomfield	—	917
Mr. Frank Cook	—	922

* *See also* Vol. 41, p. 150.

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Edited Under the Direction of the EDITORIAL COMMITTEE
Honorary Editors: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF OPHTHALMOLOGY

OFFICERS:

President—Harold Levy, F.R.C.S.

Immediate Past-President—P. E. H. Adams, F.R.C.S.

Vice-Presidents—Sir Stewart Duke-Elder, F.R.C.S.; F. W. Law, F.R.C.S.; Air Commodore P. C. Livingston, C.B.E.; A. B. Nutt, M.B.; J. D. Magor Cardell, F.R.C.S.; Charles Goulden, O.B.E., F.R.C.S.; John Marshall, M.C., M.B.

Hon. Secretaries—P. M. Moffatt, F.R.C.S.; A. Seymour Philps, F.R.C.S.

Other Members of Council—*Physicians*—R. Wyburn-Mason, M.D.; Harvey Jackson, F.R.C.S.; Macdonald Critchley, M.D.; *Metropolitan Members*—J. G. Milner, F.R.C.S.; H. B. Stallard, M.B.E., F.R.C.S.; H. M. Joseph, M.C., M.B.; A. J. B. Goldsmith, F.R.C.S.; Mary A. Pugh; B. W. Rycroft, O.B.E., F.R.C.S.; Victor Purvis, M.B.; Arthur Lister, F.R.C.S.; Hon. G. J. O. Bridgeman, M.C., F.R.C.S. *Provincial Members*—Lt.-Col. R. E. Wright, C.I.E., I.M.S.; E. G. Recordon, M.D.; Dorothy R. Campbell, M.B.; J. P. Lloyd, F.R.C.S.; G. T. Willoughby Cashell, F.R.C.S.Ed.; G. I. Scott, F.R.C.S.Ed.

Representative on Library Committee—Arnold Sorsby, F.R.C.S.

Representative on Editorial Committee—E. Wolff, F.R.C.S.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Odontology

CONTENTS

PAGE
Section Volume

November 25, 1946

SEVERE INFECTIONS OF THE MANDIBLE
D. Greer Walker, M.B., M.Dent.Sc. 1 309
REGIONAL OSTEITIS FIBROSA AFFECTING THE FACIAL BONES: TWO CASES
Martin A. Rushton, M.D., L.D.S. 8 316

January 27, 1947

THE STERILIZATION OF DENTAL HANDPIECES
Warren Harvey, C. H. LeMay and C. W. Shuttleworth 11 507

February 24, 1947

THE "THREE-PLY" STRUCTURE IN FACIAL BONES
W. Warwick James, O.B.E., F.R.C.S., M.Ch. 15 511

March 24, 1947

THREE CYSTS IN THE SAME MANDIBLE, NOT OF DENTAL ORIGIN. ? SOLITARY CYSTS OR OSTEITIS FIBROSA
George T. Hankey, O.B.E., T.D., M.R.C.S., L.D.S.Eng. 19 723

April 14, 1947

DENTAL INVESTIGATIONS OF GREENLAND ESKIMOS [*Summary*]
P. O. Pedersen 22 726

May 19, 1947

UNILATERAL HYPOPLASIA OF FACE AND TEETH
Professor Evelyn C. Sprawson, M.C., D.Sc., M.R.C.S., L.D.S. 29 835
A NOTE ON TEN ROMANO-BRITISH SKULLS FROM A BURIAL GROUND AT COMPTON, BERKSHIRE
Sir Frank Colyer, K.B.E., LL.D., F.R.C.S. 31 837

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

	PAGE Section	PAGE Volume
HOLE AT THE MACULA FOLLOWING TRAUMA P. M. Moffatt, F.R.C.S.	42	818
INTRA-OCULAR SECONDARY NEOPLASM P. M. Moffatt, F.R.C.S.	42	818
RETINITIS PROLIFERANS M. L. Hine, F.R.C.S.	42	818
? COATS'S DISEASE M. L. Hine, F.R.C.S.	42	818
THROMBOPHLEBITIS RETINÆ T. Keith Lyle, M.D., M.Chir.	42	818
RELATIVE PALSY OF LEFT SUPERIOR RECTUS DUE TO LOCAL ORBITAL TRAUMA T. Keith Lyle, M.D., M.Chir.	42	818
CONGENITAL PALSY OF RIGHT SUPERIOR OBLIQUE WITH COMPENSATORY HEAD POSTURE (OCULAR TORTICOLLIS) T. Keith Lyle, M.D., M.Chir.	43	819
RIGHT SUPERIOR OBLIQUE PARALYSIS DUE TO RIGHT FOURTH CEREBRAL NERVE PALSY CAUSED BY HEAD INJURY T. Keith Lyle, M.D., M.Chir.	43	819
CHOROIDAL NEOPLASM G. G. Penman, F.R.C.S.	43	819
EALES' DISEASE G. G. Penman, F.R.C.S.	43	819
DERMOID CYST, SIMULATING NEOPLASM OF LACRIMAL GLAND G. G. Penman, F.R.C.S.	44	820
LYMPHOMA. ? DIAGNOSIS Eugene Wolff, F.R.C.S.	44	820
DERMO-LIPOMA Eugene Wolff, F.R.C.S.	44	820
DETACHED RETINA. ? TREATMENT Eugene Wolff, F.R.C.S.	44	820
RESULT OF BLASKOWICZ OPERATION FOR CONGENITAL PTOSIS Eugene Wolff, F.R.C.S.	44	820
PERIPHERAL CYSTIC DEGENERATION. ? PROGNOSIS J. G. Milner, F.R.C.S.	44	820
BILATERAL COLOBOMA OF THE OPTIC DISC H. L. Hughes, M.B., B.S., D.O.M.S. (introduced by Professor Arnold Sorsby, F.R.C.S.)	45	821
A FAMILY SHOWING ARACHNODACTYLY WITH COLOBOMATA OF LENSES AND CHOROID R. C. Davenport, F.R.C.S.	45	821
TOXOPLASMOSIS : TWO CASES Professor A. Franceschetti	45	821

June 12, 1947

DISCUSSION ON ILLUMINATION	46–52	822–828
Mr. J. G. Drummond Currie, Dr. J. W. T. Walsh	46	822
Mr. H. C. Weston	48	824
The President, Mr. F. A. Williamson-Noble, Dr. F. W. Sharpley	51	827
Mrs. Dorothy Campbell, Mr. D. V. Giri, Dr. Brian Stanford, The President	52	828

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Section of Ophthalmology

CONTENTS

PAGE
Section Volume

October 10, 1946

Denig's Operation for Trachoma : Two Cases
Noah Pines, M.B. 1 129
(A) Diabetic Cataract ; (B) Endocrine Cataract
A. Lister, F.R.C.S. 2 130
Plastic Implant into Socket
F. A. Williamson-Noble, F.R.C.S 2 130

November 14, 1946

OPHTHALMO-NEUROLOGICAL SYMPTOMS IN MALIGNANT NASOPHARYNGEAL TUMOURS. [*Summary*]
Erik Godtfredsen, M.D.Copenhagen 3 131
THE DIAGNOSIS AND TREATMENT OF TUMOURS OF THE NASOPHARYNX
E. D. D. Davis, F.R.C.S. 7 135
Ring Scotoma after Retrobulbar Neuritis
Frank W. Law, F.R.C.S. 10 138
Denig's Operation : Two Cases
Noah Pines, M.B. 11 139
Retinal Hæmorrhage with Mitral Incompetence
Noah Pines, M.B. 12 140

December 13, 1946

Meeting Held at Manchester Royal Eye Hospital

ISOLATED OCULOMOTOR PALSY CAUSED BY INTRACRANIAL ANEURYSM
Geoffrey Jefferson, C.B.E., M.S., F.R.S. 13 419
List of Cases shown 26 432

February 13, 1947

List of Cases shown 27 569
Megalocornea (Genealogical Table)
H. E. Hobbs, F.R.C.S. 27 569
DISCUSSION ON RADIOTHERAPY IN THE TREATMENT OF NON-MALIGNANT SUPERFICIAL EYE LESIONS 28–35 570–577
Mr. R. Affleck Greeves 28 570
Professor B. W. Windeyer 29 571
Dr. M. Lederman 31 573
Mr. A. J. Durden Smith.. .. .. 34 576
Dr. N. S. Finzi, Mr. Eugene Wolff, Dr. B. Thorne-Thorne, Professor Windeyer, Dr. M. Lederman 35 577

March 13, 1947

DISCUSSION ON ALLERGY IN OPHTHALMOLOGY 36–40 578–582
Mr. Gayer Morgan, Dr. C. J. C. Britton 36 578
Dr. J. T. Ingram 37 579
Mr. Eugene Wolff, Dr. Eric Lipman Cohen, Dr. E. Felix 39 581
Dr. Vera Walker, Dr. D. Harley, Mr. Gayer Morgan, Dr. C. J. C. Britton, Dr. J. T. Ingram 40 582

May 8, 1947

Clinical Meeting Held at the Royal Westminster
Ophthalmic Hospital, London

Tuberculous Choroiditis
A. S. Philps, F.R.C.S. 41 817
Retinitis Proliferans
A. S. Philps, F.R.C.S. 41 817
Palsy of L. Inferior Oblique Muscle
A. S. Philps, F.R.C.S. 41 817
Asthma, Eczema, Cataract
A. S. Philps, F.R.C.S. 41 817
Intra-ocular Foreign Body, Non-magnetic
P. M. Moffatt, F.R.C.S. 41 817
Familial Macular Degeneration, Adolescent Type
P. M. Moffatt, F.R.C.S. 42 818

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF ORTHOPÆDICS

OFFICERS:

President—V. H. ELLIS, F.R.C.S.

Vice-Presidents—W. B. FOLEY, F.R.C.S.; ERIC I. LLOYD, F.R.C.S.; S. ALAN S. MALKIN, F.R.C.S.Ed.

Honorary Secretaries—DAVID TREVOR, M.S.; J. A. CHOLMELEY, F.R.C.S.

Other Members of Council—A. S. BLUNDELL BANKART, M.Ch.; J. S. BATCHELOR, F.R.C.S.; H. J. BURROWS, F.R.C.S.; E. S. EVANS, F.R.C.S.; A. ROCYN JONES, F.R.C.S.; H. H. LANGSTON, F.R.C.S.; M. C. WILKINSON, M.S.; H. L.-C. WOOD, M.S.

Representative on Library Committee—S. L. HIGGS, F.R.C.S.

Representative on Editorial Committee—A. M. A. MOORE, F.R.C.S.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1
1947

Printed by
STAPLES PRESS LIMITED
at their
Great Titchfield Street, London, establishment

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF OTOLOGY

OFFICERS:

President—H. V. FORSTER, M.C., M.B.

Immediate Past-President—A. J. WRIGHT, F.R.C.S.

Past-Presidents—W. M. MOLLISON, C.B.E., M.Ch.; F. C. ORMEROD, F.R.C.S.; F. W. WATKYN-THOMAS, F.R.C.S.

Vice-Presidents—MYLES FORMBY, F.R.C.S.; J. ANGELL JAMES, F.R.C.S.; C. P. WILSON, C.V.O., F.R.C.S.

Hon. Secretaries—J. F. SIMPSON, F.R.C.S.; ROYDON PEACOCK, F.R.C.S.

Other Members of Council—W. H. BRADBEER, M.S.; T. A. CLARKE, F.R.C.S.Ed.; R. L. FLETT, F.R.C.S.; J. C. HOGG, F.R.C.S.; I. SIMSON HALL, F.R.C.S.Ed.; GAVIN LIVINGSTONE, F.R.C.S.; J. PARRY MONKHOUSE, F.R.C.S.; IAN G. ROBIN, F.R.C.S.; R. R. S. STRANG, F.R.C.S.

Representative on Library Committee—C. P. WILSON, C.V.O., F.R.C.S.

Representative on Editorial Committee—C. S. HALLPIKE, F.R.C.S.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Orthopædics

CONTENTS

PAGE
Section *Volume*

October 1, 1946

INJURIES OF THE CERVICAL VERTEBRÆ
President's Address by V. H. Ellis, F.R.C.S. 1 19

November 5, 1946

PROTRUSION OF INTERVERTEBRAL DISCS
R. H. Young, F.R.C.S. 9 233
THE CROSSED TRIFIN NAIL AND GRAFT IN THE TREATMENT OF FRACTURES OF THE NECK OF THE FEMUR
G. K. McKee, F.R.C.S. 12 236
INTERTROCHANTERIC OSTEOTOMY FOR THE TREATMENT OF TUBERCULOSIS OF THE HIP
M. C. Wilkinson, M.B. 14 238
SOME POINTS ABOUT THE MONTEGGIA FRACTURE
W. Sayle Creer, F.R.C.S. 17 241

December 3, 1946

Diaphyseal Aclasis
G. O. Tippett, F.R.C.S. 19 485
Cyst in the Femur
G. O. Tippett, F.R.C.S. 19 485
Typhoid Osteitis of the Long Bones
E. T. Bailey, F.R.C.S. 20 486
Osteo-arthritis of the Hip-joint treated by Intra-articular Injections
H. Warren Crowe, D.M. 20 486
Osteoid-Osteoma of Upper End of Ulna
D. Wainwright, F.R.C.S.Ed. 21 487
Treatment of Displacements of the Distal Radio-ulnar Joint
F. P. Fitzgerald, F.R.C.S. 22 488
Chondro-osteodystrophy. ? Morquio
J. A. Cholmeley, F.R.C.S. 25 491
Osteo-arthritis of the Trapezio-metacarpal Joint treated by Excision of the Trapezium
W. H. Gervis, F.R.C.S. 26 492

February 4, 1947

DISCUSSION ON PAIN IN THE UPPER LIMB, EXCLUDING SHOULDER LESIONS 26–32 492–498
Dr. Wilfred Harris 26 492
Mr. David Le Vay 28 494
Dr. Frank A. Elliott 30 496
Dr. J. W. Aldren Turner, Mr. W. E. Tucker 32 498

March 4, 1947

List of Cases shown 33 885

May 6, 1947

RECURRENT DISLOCATION OF THE ELBOW-JOINT
D. Wainwright, F.R.C.S.Ed. 33 885
PSEUDOCOXALGIA: (CALVÉ-LEGG-PERTHES' DISEASE). THE RADIOGRAPHIC CHANGES OUTSIDE THE FEMORAL HEAD
H. G. Korvin, F.R.C.S. 34 886

June 21, 1947

BRIEF NOTE ON THE CONTRIBUTIONS OF THE LATE SIR HENRY GAUVAIN TO ORTHOPÆDIC SURGERY
Sir Thomas Fairbank 40 892
CASES AND CASE RECORDS ILLUSTRATING ORTHOPÆDIC AND PLASTIC SURGICAL TEAM WORK
Professor T. Pomfret Kilner, C.B.E., F.R.C.S. 40 892
THE BRITTAIN METHOD OF ARTHRODESIS OF THE HIP
H. H. Langston, F.R.C.S. 43 895

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF PÆDIATRICS

(*Previously* SECTION FOR THE STUDY OF DISEASE IN CHILDREN)

OFFICERS:

President—DENIS BROWNE, F.R.C.S.

Vice-Presidents—NORMAN CAPON, M.D.; ERIC A. CROOK, M.Ch.; HELEN MACKAY, F.R.C.P.

Hon. Secretaries—CHARLES PINCKNEY, F.R.C.P.; PHILIP EVANS, M.R.C.P.

Other Members of Council—A. DOYNE BELL, D.M.; R. E. BONHAM CARTER, M.R.C.P.; R. W. B. ELLIS, O.B.E., M.D.; D. M. T. GAIRDNER, M.R.C.P.; WILLIAM GUNN, M.B.; G. H. NEWNS, M.D.; T. S. RODGERS, M.D.; J. M. SMELLIE, O.B.E., M.D.; K. H. TALLERMAN, M.C., M.D.; MARY WILMERS, M.D.

Representative on Library Committee—A. WHITE FRANKLIN, F.R.C.P.

Representative on Editorial Committee—A. G. SIGNY, M.B.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Otology

CONTENTS

PAGE
Section *Volume*

November 1, 1946

OTOLOGY IN SCHOOL CHILDREN AND CHILD WELFARE
President's Address by H. V. Forster, M.C., M.B., Ch.B., M.Sc. 1 101

December 6, 1946

TECHNIQUE OF FENESTRATION OPERATION
Mr. E. R. Garnett Passe 9 319
BILATERAL CLINICAL OTOSCLEROSIS TREATED BY THE FENESTRATION OPERATION USING THE CARTILAGE STOPPLE AND THE ENDAURAL APPROACH
E. R. Garnett Passe, F.R.C.S. 9 319
AN OPERATING MICROSCOPE FOR THE FENESTRATION OPERATION
J. F. Simpson, F.R.C.S. 10 320
REVIEW OF SURGERY OF OTOSCLEROSIS
Terence Cawthorne, F.R.C.S. 10 320

February 7, 1947

TRANSMEATAL ATTICO-ANTROTOMY IN CHRONIC TYMPANO-MASTOID SUPPURATION
A. Tumarkin, F.R.C.S.Ed. 19 761

SECTION OF OTOLOGY WITH SECTION OF LARYNGOLOGY

COMBINED SUMMER MEETING HELD IN BRIGHTON

LARYNGOLOGICAL SESSION

June 27, 1947

CERTAIN ANATOMICAL AND PHYSIOLOGICAL CONSIDERATIONS IN PARALYSIS OF THE LARYNX
V. E. Negus 27 849
THE TREATMENT OF SUBACUTE MAXILLARY SINUSITIS ESPECIALLY IN CHILDREN
G. E. Archer 32 854
FILM: "BRONCHIAL NEOPLASMS"
Paul H. Holinger, Chicago (shown by G. H. Bateman) 36 858

(For Otological Session *see* Vol. 41, p. 1.)

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

March 28, 1947

	PAGE Section	PAGE Volume
DISCUSSION ON ANÆSTHESIA IN CHILDREN	20–24	540–544
Dr. R. W. Cope	20	540
Dr. D. Aserman	22	542
Dr. I. W. Magill	24	544

April 18, 1947

MEETING HELD AT THE HOSPITAL FOR SICK CHILDREN,
GREAT ORMOND STREET, LONDON, W.C.1

DIABETES INSIPIDUS B. W. Powell, M.B., M.R.C.P. (for Bernard Schlesinger, F.R.C.P.)	24	544
NEPHRITIS WITH ŒDEMA B. W. Powell, M.B., M.R.C.P. (for Bernard Schlesinger, F.R.C.P.)	24	544
HYPOPLASTIC ANÆMIA I. A. B. Cathie, M.D.	25	545
STURGE-WEBER SYNDROME N. F. Elliott Burrows, B.M. (for W. G. Wyllie, M.D.)	26	546
EXOPHTHALMIC GOITRE J. M. Alexander, M.R.A.C.P. (for W. G. Wyllie, M.D.)	26	546
NEUROFIBROMATOSIS J. M. Alexander, M.R.A.C.P. (for W. G. Wyllie, M.D.)	26	546
PSEUDO-HYPERTROPHIC MUSCULAR DYSTROPHY J. M. Alexander, M.R.A.C.P. (for W. G. Wyllie, M.D.)	26	546

May 23, 1947

ERYTHROBLASTOSIS FŒTALIS OR HÆMOLYTIC DISEASE OF THE NEWBORN. [*Abstract of Illustrated Talk*] Louis K. Diamond, M.D.	26	546

June 14, 1947

MEETING HELD AT ROYAL VICTORIA INFIRMARY,
NEWCASTLE UPON TYNE

List of papers read	30	550

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Section of Pædiatrics

CONTENTS

October 25, 1946

PAGE
Section *Volume*

KALA-AZAR IN INFANCY
Professor J. E. Debono (*Malta*) 1 155

November 22, 1946

THYROTOXICOSIS IN A CHILD AGED 2 YEARS 9 MONTHS
Gerald Slot, M.D. 5 159
CALCINOSIS UNIVERSALIS
A. P. Norman, M.B. (for Donald Paterson, F.R.C.P.) 6 160
SCLEREMA
A. P. Norman, M.B. (for Donald Paterson, F.R.C.P.) 6 160
CONGENITAL SYPHILIS
J. Heber, M.B., B.S. (for Mary Wilmers, M.D.) 7 161
TUBERCULOUS ABSCESS FORMATION FOLLOWING PENICILLIN THERAPY
P. J. Coope, M.B. (for J. C. R. Hindenach, F.R.C.S.) 7 161
JUVENILE CIRRHOSIS
Ursula James, M.B., M.R.C.P. 8 162
HEPATOSPLENOMEGALY: FOR DIAGNOSIS
C. F. Saunders, L.R.C.P., M.R.C.S. (for Philip Evans, F.R.C.P.) 9 163
INTRACRANIAL HÆMANGIOMA CAUSING CONVULSIONS
M. W. West, M.B. (introduced by R. C. Lightwood, M.D.) 10 164
ANGIOMA OF THE BASAL GANGLIA
L. J. Rowley, M.B. (for Donald Paterson, F.R.C.P., and Wylie McKissock, O.B.E., M.S.) 10 164
STAPHYLOCOCCAL PNEUMONIA WITH OBSTRUCTIVE EMPHYSEMA
L. G. Scott, M.B., B.S. (for Donald Paterson, F.R.C.P.) 11 165
SPONTANEOUS BILATERAL PNEUMOTHORAX OCCURRING IN A PREMATURE BABY DURING THE NEO-NATAL PERIOD
Jean W. Paul, M.B. (for S. Yudkin, M.R.C.P.) 11 165
OXYCEPHALY
Philip Evans, M.D. 12 166

February 28, 1947

LIPODYSTROPHY
M. E. MacGregor, M.D. (for Ursula James, M.R.C.P.) 13 533
CONGENITAL DEFECT OF THE SCALP
Simon Yudkin, M.B., M.R.C.P. (for H. M. M. Mackay, M.D., F.R.C.P.) 13 533
PNEUMATOCŒLE OCCURRING DURING PNEUMONIA AND RUPTURING TO FORM A PNEUMOTHORAX
Josephine Heber, M.B. (for H. M. M. Mackay, M.D., F.R.C.P.) 14 534
TRAUMATIC PERIOSTITIS
R. M. Todd, M.D., M.R.C.P., D.C.H. 15 535
HYPERELASTICITY OF SKIN
E. M. Kingsley Pillers, M.B. (for Richard Dobbs, M.R.C.P.) 17 537
CYSTIC DISEASE OF BONE
N. F. Elliott Burrows, B.M. (for Bernard Schlesinger, F.R.C.P.) 18 538
HEPATOSPLENOMEGALY
J. P. M. Tizard, B.M., M.R.C.P. (for Donald Paterson, F.R.C.P.) .. 18 538
DEMONSTRATION: DIAGNOSIS OF *THREADWORMS*
J. M. Watson, D.Sc., A.R.C.S., and R. C. Mac Keith, D.M., M.R.C.P. .. 19 539

PROCEEDINGS

OF THE

ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF PATHOLOGY

OFFICERS:

President—A. B. ROSHER, M.R.C.S., L.R.C.P., D.P.H.

Immediate Past-President—W. G. BARNARD, F.R.C.P.

Vice-Presidents—A. B. BRATTON, D.S.O., M.B.; J. M. ALSTON, M.R.C.P.Ed.; A. W. DOWNIE, M.D.; F. R. SELBIE, M.D.

Hon. Secretaries—G. PAYLING WRIGHT, D.M.; R. CRUICKSHANK, M.D.

Other Members of Council—S. P. BEDSON, M.D., F.R.S.; J. H. DIBLE, M.B.; A. N. DRURY, C.B.E., M.D., F.R.S.; C. H. ANDREWES, M.D., F.R.S.; L. P. GARROD, M.D.; G. W. GOODHART, M.D.; A. HADDOW, M.D.; J. W. ORR, M.D.; D. M. PRYCE, M.D.; JOAN M. ROSS, M.D.; A. A. MILES, M.R.C.P.; E. W. TODD, M.D.

Representative on Library Committee—J. McINTOSH, M.D.

Representative on Editorial Committee—R. W. SCARFF, M.B.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Printed by
STAPLES PRESS LIMITED
at their
Great Titchfield Street, London, establishment

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF PHYSICAL MEDICINE

OFFICERS:

President—FRANK COOKSEY, O.B.E., M.D.

Immediate Past-President—J. W. T. PATTERSON, M.D.

Vice-Presidents—L. D. BAILEY, C.B.; P. BAUWENS; E. J. CRISP, M.B.; G. D. KERSLEY, M.D.; G. K. STONE, M.D.

Hon. Secretaries—BASIL KIERNANDER, M.R.C.P.; H. F. TURNEY, D.M.

Other Members of Council—FRANCIS BACH, M.D.; DORIS BAKER, M.D.; HUGH BURT, M.R.C.P.; LEONARD BOYS, M.B.; A. R. NELIGAN, M.D.; AGNES SAVILL, M.D.; J. SHULMAN, M.B.

Representative on Library Committee—Sir ROBERT STANTON WOODS, M.D.

Representative on Editorial Committee—M. B. RAY, D.S.O., M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Pathology

CONTENTS

December 17, 1946

	PAGE *Section*	 *Volume*
DISCUSSION ON THROMBOSIS	1–8	193–200
Mr. H. J. B. Atkins: *Post-operative thrombosis*	1	193
Dr. R. H. D. Short: *Pathology of primary or idiopathic thrombosis of the leg veins*	3	195
Dr. Helen Wright: *Blood findings*	5	197

March 18, 1947

DISCUSSION: THE LABORATORY DIAGNOSIS OF VIRUS INFECTIONS	9–20	657–668
Professor A. W. Downie: *Laboratory diagnosis of smallpox*	9	657
Dr. J. A. Dudgeon: *Laboratory diagnosis of influenza*	12	660
Professor S. P. Bedson: *Psittacosis-lymphogranuloma group*	14	662
Dr. F. O. MacCallum: *Neurotropic viruses*	17	665

October 21, 1947

HÆMOPHILUS INFLUENZÆ AND ITS RELATION TO EPIDEMIC INFLUENZA President's Address by A. B. Rosher, M.R.C.S., L.R.C.P., D.P.H.	21	749

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Edited Under the Direction of the EDITORIAL COMMITTEE
Honorary Editors: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF PHYSICAL MEDICINE

OFFICERS:

President—Frank Cooksey, O.B.E., M.D.

Immediate Past-President—J. W. T. Patterson, M.D.

Vice-Presidents—L. D. Bailey, C.B.; P. Bauwens; E. J. Crisp, M.B.; G. D. Kersley, M.D.; G. K. Stone, M.D.

Hon. Secretaries—Basil Kiernander, M.R.C.P.; H. F. Turney, D.M.

Other Members of Council—Francis Bach, M.D.; Doris Baker, M.D.; Hugh Burt, M.R.C.P.; Leonard Boys, M.B.; A. R. Neligan, M.D.; Agnes Savill, M.D.; J. Shulman, M.B.

Representative on Library Committee—Sir Robert Stanton Woods, M.D.

Representative on Editorial Committee—M. B. Ray, D.S.O., M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Physical Medicine

CONTENTS

PAGE
Section *Volume*

November 13, 1946

PHYSIOTHERAPY IN AN ACCIDENT SERVICE
Sir Max Page, K.B.E., C.B., M.S. 1 15

January 8, 1947

REHABILITATION IN CHEST INJURY 5–10 287–292
Mr. T. Holmes Sellors 5 287
Dr. William M. MacPhail 9 291

February 12, 1947

CLINICAL MEETING AT THE LONDON HOSPITAL, E.1.

List of Cases shown 11 293

March 12, 1947

ANALYSIS OF FUNCTION
H. Ernest Griffiths, C.B.E., M.S., F.R.C.S. 11 293

April 9, 1947

SAMUEL HYDE MEMORIAL LECTURE:

RHEUMATIC DISEASES: A CHALLENGE AND AN OPPORTUNITY
Professor Henry Cohen, M.D., F.R.C.P. 19 443

June 18, 1947

THE COMPLEX BEHAVIOUR OF HIGH-FREQUENCY CURRENTS IN SIMPLE CIRCUITS
P. Bauwens, M.R.C.S., L.R.C.P. 29 741

SECTION OF MEDICINE WITH SECTION OF PHYSICAL MEDICINE
(*JOINT DISCUSSION No.* 1)

January 28, 1947

THE ÆTIOLOGY OF CHRONIC RHEUMATISM .. .. — 329–346
Dr. W. S. C. Copeman .. .. — 329
Dr. Philip Ellman .. .. — 332
Dr. G. D. Kersley .. .. — 343
Dr. Ernest Fletcher, Dr. W. R. Thrower, Dr. W. Annandale Troup .. — 345
Dr. W. Ganado .. .. — 346

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF PROCTOLOGY

OFFICERS:

President—A. HEDLEY WHYTE, M.S.

Immediate Past-President—ERIC A. CROOK, M.Ch.

Vice-Presidents—R. S. CORBETT, M.Ch.; CUTHBERT E. DUKES, O.B.E., M.D.; J. P. LOCKHART-MUMMERY, F.R.C.S.; W. ERNEST MILES, F.R.C.S.; E. T. C. MILLIGAN, O.B.E., F.R.C.S.; G. GREY TURNER, M.S.

Honorary Secretaries—ALAN HUNT, F.R.C.S.; RONALD RAVEN, O.B.E., F.R.C.S.

Other Members of Council—A. LAWRENCE ABEL, M.S.; HAROLD DODD, F.R.C.S.; W. B. GABRIEL, M.S.; KENNETH JAMES, M.S.; C. NAUNTON MORGAN, F.R.C.S.; E. G. MUIR, M.S.; Sir HENEAGE OGILVIE, K.B.E., M.Ch.; A. DICKSON WRIGHT, M.S.

Representative on Library Committee—LIONEL E. C. NORBURY, O.B.E., F.R.C.S.

Representative on Editorial Committee—O. V. LLOYD-DAVIES, M.S.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Proctology

CONTENTS

PAGE
Section *Volume*

November 20, 1946

PROCTOLOGY PAST AND PRESENT
President's Address by A. Hedley Whyte, D.S.O., T.D., M.S., F.R.C.S. .. 1 179

March 12, 1947

AN EXPLANATION OF THE DIFFERENCE BETWEEN A PAPILLOMA AND AN ADENOMA OF THE RECTUM
Cuthbert E. Dukes, O.B.E., M.D. 7 829
RIGHT HEMICOLECTOMY
E. G. Muir, M.S., F.R.C.S. 9 831
A Small High-grade Carcinoma of the Rectum with Extensive Lymphatic Spread
W. B. Gabriel, M.S. 11 833
Carcinoma of the Paroophoron, Invading the Rectum
A. Lawrence Abel, M.S... .. .. 12 834
Specimen of Colon Removed on Account of Severe Pyoderma from a Long-Standing Case of Chronic Ulcerative Colitis
Rupert S. Corbett, M.Ch. 13 871
ASSOCIATED CARCINOMA OF COLON AND RECTUM. REPORT OF TWO CASES
Frank Forty, M.B., B.S., F.R.C.S. 14 872
Carcinoma of the Cæcum associated with Carcinoid Tumour of the Small Intestine
C. Naunton Morgan, F.R.C.S. 16 874
Carcinoma of the Rectum with a Single Secondary in the Liver. Synchronous Combined Excision and Left Hepatectomy
O. V. Lloyd-Davies, M.S. 17 875
Partial Hepatectomy and Right Hemicolectomy for Carcinoma of the Hepatic Flexure of the Colon
Ronald W. Raven, O.B.E., F.R.C.S. 18 876

May 14, 1947

DISCUSSION ON CONGENITAL ANOMALIES OF THE ANORECTAL REGION 18–22 876–880
Professor John Kirk 18 876
Professor R. A. Willis 21 879

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF PSYCHIATRY

OFFICERS:

President—AUBREY LEWIS, M.D.

Vice-Presidents—D. K. HENDERSON, F.R.C.P.Ed., F.R.S.E.; R. M. STEWART, M.D.; J. R. REES, C.B.E., F.R.C.P.

Honorary Secretaries—R. STRÖM-OLSEN, M.D.; DENIS HILL, M.R.C.P.

Other Members of Council—M. B. BRODY, M.D.; E. CUNNINGHAM DAX; Sir NORWOOD EAST, F.R.C.P.; E. GUTTMANN, M.D.; J. S. HARRIS, M.D.; R. E. HEMPHILL, M.D.; G. W. B. JAMES, M.C., M.D.; MAXWELL JONES, M.R.C.P.Ed.; S. A. MACKEITH, O.B.E.; W. S. MACLAY, O.B.E., M.D.; EMANUEL MILLER, M.D.; SYLVIA PAYNE, C.B.E., M.B.; G. DE M. RUDOLF, M.R.C.P.; WILLIAM SARGANT, M.R.C.P.; A. F. TREDGOLD, M.D.

Representative on Library Committee—A. B. STOKES, C.B.E., M.R.C.P.

Representative on Editorial Committee—R. STRÖM-OLSEN, M.D.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Psychiatry

CONTENTS

PAGE
Section Volume

November 12, 1946

THE MEASUREMENT OF PERSONALITY. [*Résumé*]
H. J. Eysenck, Ph.D.London 1 75

December 10, 1946

DISCUSSION: LEUCOTOMY AS AN INSTRUMENT OF RESEARCH 7–16 141–150
Dr. A. Meyer and Dr. T. McLardy 7 141
Dr. G. D. Greville and Dr. S. L. Last 11 145
Dr. F. Reitman 13 147
Dr. M. B. Brody 15 149

January 14, 1947

THE MORPHOLOGICAL LEVEL OF PERSONALITY
J. M. Tanner, M.B., D.P.M.Lond., M.D.Penn. 17 301

March 11, 1947

DISORDERS OF SKILL: AN EXPERIMENTAL APPROACH TO SOME PROBLEMS OF NEUROSIS. [*Abstract*]
D. Russell Davis, M.D., M.R.C.P., D.P.M. 25 583

April 8, 1947

DISCUSSION ON THE SOCIAL ASPECTS OF HOMOSEXUALITY. [*Summary*] 27–34 585–592
Dr. E. A. Bennet 27 585
Dr. H. Mannheim 29 587
Dr. D. Stanley-Jones 30 588
Sir Norwood East 32 590
Dr. John C. Mackwood 33 591

June 10, 1947

THE IMPORTANCE OF STATISTICS IN PSYCHIATRY
L. S. Penrose, M.D. 35 863

The Society does not in any way hold itself responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

Edited Under the Direction of the EDITORIAL COMMITTEE
Honorary Editors: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
Assistant Editor: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF RADIOLOGY

OFFICERS:

President—Whately Davidson, M.D.

Immediate Past-President—W. M. Levitt, M.D.

Vice-Presidents—Frank Ellis, M.D.; Peter Kerley, M.D.; J. Ralston Paterson, M.C., F.R.C.S.Ed.; J. V. Sparks; G. F. Stebbing, F.R.C.S.; E. Rohan Williams, M.D.

Hon. Secretaries—J. A. C. Fleming, F.R.C.S.Ed.; R. A. Kemp Harper, M.B.

Other Members of Council—S. B. Adams, M.D.; J. F. Bromley, O.B.E., M.B.; G. B. Bush, M.B.; G. T. Calthrop, M.D.; Hugh Davies, D.M.; R. Fawcitt, M.D.; N. S. Finzi, M.B.; E. Duff Gray, M.D.; M. C. Tod, F.R.C.S.Ed.; I. G. Williams, F.R.C.S.; B. W. Windeyer, F.R.C.S.Ed.; Charles Wroth.

Representative on Library Committee—F. Campbell Golding, M.B.

Representative on Editorial Committee—F. Campbell Golding, M.B.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Radiology

CONTENTS

PAGE
Section Volume

November 15, 1946

DISCUSSION: THE X-RAY TREATMENT OF INFLAMMATORY DISEASES .. 1–8 109–116
Dr. Mary Cripps .. 1 109
Dr. Alfreda H. Baker .. 3 111
Dr. Francis Freund .. 5 113
Dr. N. S. Finzi .. 7 115

January 17, 1947

VALUE OF TOMOGRAPHY IN LESIONS OF THE MAIN BRONCHI AND THEIR LARGER SUB-DIVISIONS
Stanley Nowell, M.B., F.F.R., D.M.R. .. 9 399
DISSEMINATED OSSIFIED NODULES IN THE LUNGS ASSOCIATED WITH MITRAL STENOSIS
A. Elkeles, M.D. .. 15 405

February 21, 1947

CARCINOMA OF THE THYROID
J. M. Graham, P.R.C.S.Ed., and R. McWhirter, F.R.C.S.Ed. .. 19 669

March 21, 1947

SOME EXPERIENCES WITH BONE TUMOURS. [*Abridged*]
James F. Brailsford, M.D., Ph.D., F.R.C.P., F.I.C.S. .. 31 787

SECTION OF SURGERY WITH SECTION OF RADIOLOGY

(*JOINT DISCUSSION No.* 2)

January 1, 1947

DISCUSSION ON THE TREATMENT OF CANCER OF THE TONGUE — 409–418
Sir Stanford Cade .. — 409
Dr. Ralston Paterson .. — 412
Mr. W. R. Douglas .. — 415
Lieut.-Colonel W. L. Harnett .. — 417
Mr. Anthony Green .. — 418

SECTION OF OBSTETRICS AND GYNÆCOLOGY WITH SECTION OF RADIOLOGY

(*JOINT DISCUSSION No.* 3)

May 16, 1947

DISCUSSION ON SOME ASPECTS OF SURGICAL AND RADIOLOGICAL TREATMENT OF CARCINOMA OF THE CERVIX .. — 907–922
Professor Subodh Mitra, F.R.C.S.Ed., F.R.C.O.G.(Calcutta) .. — 907
Mr. Charles D. Read .. — 909
G. E. Richards, M.D. (Toronto)* .. — 911
Mr. G. W. Blomfield .. — 917
Mr. Frank Cook .. — 922

* *See also* Vol. 41, p. 150.

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE

HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF SURGERY

OFFICERS:

President—E. F. FINCH, M.S.

Immediate Past-President—Sir JAMES WALTON, K.C.V.O., M.S.

Vice-Presidents—R. H. BOGGON, M.S.; RUPERT S. CORBETT, M.Ch.; ERIC A. CROOK, M.Ch.

Hon. Secretaries—VICTOR RIDDELL, F.R.C.S.; A. WALLIS KENDALL, M.S.

Other Members of Council—CHARLES DONALD, O.B.E., Ch.M.; HAROLD EDWARDS, C.B.E., M.S.; O. V. LLOYD-DAVIES, M.S.; RODNEY MAINGOT, F.R.C.S.; C. NAUNTON MORGAN, F.R.C.S.; F. A. R. STAMMERS, F.R.C.S.; W. E. TANNER, M.S.; J. R. M. WHIGHAM, M.S.

Representative on Library Committee—LIONEL E. C. NORBURY, O.B.E., F.R.C.S.

Representative on Editorial Committee—R. DAVIES-COLLEY, C.M.G., M.Ch.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Radiology

CONTENTS

November 15, 1946

	PAGE *Section*	*Volume*
DISCUSSION: THE X-RAY TREATMENT OF INFLAMMATORY DISEASES ..	1–8	109–116
Dr. Mary Cripps ..	1	109
Dr. Alfreda H. Baker	3	111
Dr. Francis Freund	5	113
Dr. N. S. Finzi ..	7	115

January 17, 1947

VALUE OF TOMOGRAPHY IN LESIONS OF THE MAIN BRONCHI AND THEIR LARGER SUB-DIVISIONS Stanley Nowell, M.B., F.F.R., D.M.R.	9	399
DISSEMINATED OSSIFIED NODULES IN THE LUNGS ASSOCIATED WITH MITRAL STENOSIS A. Elkeles, M.D. ..	15	405

February 21, 1947

CARCINOMA OF THE THYROID J. M. Graham, P.R.C.S.Ed., and R. McWhirter, F.R.C.S.Ed.	19	669

March 21, 1947

SOME EXPERIENCES WITH BONE TUMOURS. [*Abridged*] James F. Brailsford, M.D., Ph.D., F.R.C.P., F.I.C.S.	31	787

SECTION OF SURGERY WITH SECTION OF RADIOLOGY
(*JOINT DISCUSSION No.* 2)

January 1, 1947

DISCUSSION ON THE TREATMENT OF CANCER OF THE TONGUE	—	409–418
Sir Stanford Cade	—	409
Dr. Ralston Paterson	—	412
Mr. W. R. Douglas	—	415
Lieut.-Colonel W. L. Harnett ..	—	417
Mr. Anthony Green	—	418

SECTION OF OBSTETRICS AND GYNÆCOLOGY WITH SECTION OF RADIOLOGY
(*JOINT DISCUSSION No.* 3)

May 16, 1947

DISCUSSION ON SOME ASPECTS OF SURGICAL AND RADIOLOGICAL TREATMENT OF CARCINOMA OF THE CERVIX..	—	907–922
Professor Subodh Mitra, F.R.C.S.Ed., F.R.C.O.G.(Calcutta)	—	907
Mr. Charles D. Read	—	909
G. E. Richards, M.D. (Toronto)*	—	911
Mr. G. W. Blomfield	—	917
Mr. Frank Cook ..	—	922

* *See also* Vol. 41, p. 150.

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF SURGERY

OFFICERS:

President—E. F. FINCH, M.S.

Immediate Past-President—Sir JAMES WALTON, K.C.V.O., M.S.

Vice-Presidents—R. H. BOGGON, M.S.; RUPERT S. CORBETT, M.Ch.; ERIC A. CROOK, M.Ch.

Hon. Secretaries—VICTOR RIDDELL, F.R.C.S.; A. WALLIS KENDALL, M.S.

Other Members of Council—CHARLES DONALD, O.B.E., Ch.M.; HAROLD EDWARDS, C.B.E., M.S.; O. V. LLOYD-DAVIES, M.S.; RODNEY MAINGOT, F.R.C.S.; C. NAUNTON MORGAN, F.R.C.S.; F. A. R. STAMMERS, F.R.C.S.; W. E. TANNER, M.S.; J. R. M. WHIGHAM, M.S.

Representative on Library Committee—LIONEL E. C. NORBURY, O.B.E., F.R.C.S.

Representative on Editorial Committee—R. DAVIES-COLLEY, C.M.G., M.Ch.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Surgery

CONTENTS

PAGE
Section *Volume*

November 6, 1946

DISCUSSION ON THE TREATMENT OF ACUTE PERITONITIS .. 1–6 123–128
Mr. John Morley 1 123
Mr. C. G. Rob 4 126
Mr. R. Vaughan Hudson 6 128

February 5, 1947

DISCUSSION ON TREATMENT OF NON-TUBERCULOUS EMPYEMA 7–14 645–652
Mr. R. C. Brock 7 645
Mr. T. Holmes Sellors 11 649

March 5, 1947

THE PACKING OF ABDOMINAL INCISIONS IN PERITONITIS
Ivor Lewis, M.S. 14 652
THE CONCENTRATION OF PENICILLIN IN BILE
E. G. Tuckwell, F.R.C.S. 16 654

April 2, 1947

TECHNIQUE AND VALUE OF TATTOOING IN PLASTIC SURGERY
D. N. Matthews, O.B.E., M.Ch., F.R.C.S. 19 881

May 3, 1947

MEETING HELD AT THE ROYAL HOSPITAL, SHEFFIELD

SOME DERMATOLOGICAL COMPLICATIONS OF OPEN WOUNDS
I. B. Sneddon, M.B., Ch.B., M.R.C.P. 21 883

SECTION OF SURGERY WITH SECTION OF RADIOLOGY
(JOINT DISCUSSION No. 2)

January 1, 1947

DISCUSSION ON THE TREATMENT OF CANCER OF THE TONGUE — 409–418
Sir Stanford Cade .. .. — 409
Dr. Ralston Paterson .. .. — 412
Mr. W. R. Douglas .. .. — 415
Lieut.-Colonel W. L. Harnett .. .. — 417
Mr. Anthony Green .. .. — 418

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

PROCEEDINGS
OF THE
ROYAL SOCIETY OF MEDICINE

EDITED UNDER THE DIRECTION OF THE EDITORIAL COMMITTEE
HONORARY EDITORS: MAURICE DAVIDSON, M.D., and ERIC A. CROOK, M.Ch.
ASSISTANT EDITOR: J. M. BROWNE KUTSCHBACH, M.B., D.P.H.

VOLUME THE FORTIETH. *SESSION* 1946-47

SECTION OF UROLOGY

OFFICERS:

President—R. H. O. B. ROBINSON, F.R.C.S.

Immediate Past-President—A. WILFRID ADAMS, M.S.

Vice-Presidents—HUGH DONOVAN, F.R.C.S.; KENNETH HERITAGE, M.S.

Hon. Secretaries—J. C. AINSWORTH-DAVIS, F.R.C.S.; EDGAR FRESHMAN, F.R.C.S.

Other Members of Council—A. W. BADENOCH, F.R.C.S.; J. D. FERGUSSON, F.R.C.S.; W. H. GRAHAM, F.R.C.S.; T. J. MILLIN, M.Ch.; T. W. MIMPRISS, M.S.; R. W. REID, F.R.C.S.; J. G. SANDREY, F.R.C.S.; R. OGIER WARD, D.S.O., M.Ch.

Representative on Library Committee—E. W. RICHES, M.C., M.S.

Representative on Editorial Committee—A. CLIFFORD MORSON, O.B.E., F.R.C.S.

LONDON
LONGMANS, GREEN & CO., LTD., 6 & 7, CLIFFORD STREET, W.1.
1947

Section of Surgery

CONTENTS

PAGE

November 6, 1946

	Section	Volume
DISCUSSION ON THE TREATMENT OF ACUTE PERITONITIS	1–6	123–128
Mr. John Morley	1	123
Mr. C. G. Rob	4	126
Mr. R. Vaughan Hudson	6	128

February 5, 1947

	Section	Volume
DISCUSSION ON TREATMENT OF NON-TUBERCULOUS EMPYEMA	7–14	645–652
Mr. R. C. Brock	7	645
Mr. T. Holmes Sellors	11	649

March 5, 1947

	Section	Volume
THE PACKING OF ABDOMINAL INCISIONS IN PERITONITIS Ivor Lewis, M.S.	14	652
THE CONCENTRATION OF PENICILLIN IN BILE E. G. Tuckwell, F.R.C.S.	16	654

April 2, 1947

	Section	Volume
TECHNIQUE AND VALUE OF TATTOOING IN PLASTIC SURGERY D. N. Matthews, O.B.E., M.Ch., F.R.C.S.	19	881

May 3, 1947

Meeting Held at the Royal Hospital, Sheffield

	Section	Volume
SOME DERMATOLOGICAL COMPLICATIONS OF OPEN WOUNDS I. B. Sneddon, M.B., Ch.B., M.R.C.P.	21	883

SECTION OF SURGERY WITH SECTION OF RADIOLOGY
(*JOINT DISCUSSION No.* 2)

January 1, 1947

	Section	Volume
DISCUSSION ON THE TREATMENT OF CANCER OF THE TONGUE	—	409–418
Sir Stanford Cade	—	409
Dr. Ralston Paterson	—	412
Mr. W. R. Douglas	—	415
Lieut.-Colonel W. L. Harnett	—	417
Mr. Anthony Green	—	418

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

Section of Comparative Medicine

President—Professor G. R. Cameron, F.R.C.P., F.R.S.

[*October 16, 1946*]

Sudden Shifts of Body Fluids

PRESIDENT'S ADDRESS

By Professor G. R. Cameron, F.R.C.P., F.R.S.

Amongst the many unsolved problems of physiology and pathology is the fascinating one of re-distribution of body fluids when something goes wrong with the vessels and tissue spaces in which these fluids are normally contained. During the war period I had occasion to study this question from an unusual viewpoint, that of chemical warfare. I make no apology for the choice as a Presidential Address of what at first seems a highly specialized matter, for it will, I hope, become apparent that the focus of all such researches is one common to Medicine in its widest sense. Resolution of the problem will bring the answer to many difficulties, too often regarded as practical in contra-distinction to academic, an attitude I hold to be quite wrong.

When a highly irritant liquid such as lewisite or mustard gas is dropped on the skin in minute droplets, a blister forms in a few hours. The nature of this familiar disturbance is well known. It consists in the partial or complete separation of the avascular epidermis from the underlying vascular dermis by a fluid, at first free from cellular content but later fairly rich in white blood corpuscles. This fluid invariably contains other components of the blood, especially proteins and various salts. Sometimes the protein is in large amounts and may even approach a concentration of 6%, which means that the fluid is almost pure plasma from the circulating blood. The distribution of salts can be shown to obey the predictions which follow from a Gibbs-Donnan equilibrium and as such can be dismissed from this discussion without further comment. The epidermal covering or dome of the blister is so vitiated by the action of the causative agent and no doubt, too, by its separation from its nutritive bed, the dermis, that it invariably dies and later separates at the edges of attachment, thus presenting a problem to the surviving healthy structures around, a problem which is solved in the process we call regeneration. Two important features characterize the formation of such a blister, (1) the localized outpouring of blood plasma from the blood-vessels of the affected part, and (2) the detachment of the epidermis by this rush outwards of plasma. We know a good deal about the first mechanism, but very little about the second, although the important researches of Peters and his colleagues, and of Medawar, hold out promise of a solution in the discovery of proteolytic enzymes liberated after skin damage which may be responsible for loosening of the basement membrane which anchors the epidermis to the dermis.

Experimental pathology has long known that outpouring of a fluid follows injury by various means of blood-vessels, especially capillaries. There is an impressive

Section of Urology

CONTENTS

PAGE
Section *Volume*

November 28, 1946

SOME PROBLEMS OF RENAL LITHIASIS
President's Address by R. H. O. B. Robinson, F.R.C.S. 1 201

January 23, 1947

List of Cases and Specimens shown 19 433

February 27, 1947

DISCUSSION ON THE USE OF PENICILLIN IN UROLOGY 19–28 433–442
Dr. A. L. P. Peeney 19 433
Lady Florey 26 440
Mr. Clifford Morson, Mr. Yates Bell 27 441
Mr. Edgar Freshman, Mr. Hugh Donovan 28 442

March 27, 1947

INJURIES TO THE BLADDER
Richard A. Mogg, F.R.C.S. 29 795
INJURIES OF THE URETHRA. [*Abridged*]
D. S. Poole-Wilson, F.R.C.S. 32 798
SOME OBSERVATIONS ON A PERSONAL SERIES OF BATTLE CASUALTIES INVOLVING THE GENITO-URINARY SYSTEM. [*Abridged*]
Geoffrey E. Parker, F.R.C.S. 38 804

April 24, 1947

TREATMENT OF HYDRONEPHROSIS ASSOCIATED WITH ABNORMAL VESSELS
H. Hamilton Stewart, F.R.C.S. 41 807

May 22, 1947

CLINICO-PATHOLOGICAL MEETING HELD AT ST. THOMAS'S HOSPITAL, LONDON, S.E.1

List of Cases and Specimens shown 43 809

June 26, 1947

List of Cases and Specimens shown 43 809
SURVIVAL OF A TESTICLE TRANSPLANTED INTO SCARPA'S TRIANGLE
R. Ogier Ward, D.S.O., M.Ch... .. .. 44 810

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

Section of Comparative Medicine

President—Professor G. R. CAMERON, F.R.C.P., F.R.S.

October 16, 1946

Sudden Shifts of Body Fluids

PRESIDENT'S ADDRESS

By Professor G. R. CAMERON, F.R.C.P., F.R.S.

AMONGST the many unsolved problems of physiology and pathology is the fascinating one of re-distribution of body fluids when something goes wrong with the vessels and tissue spaces in which these fluids are normally contained. During the war period I had occasion to study this question from an unusual viewpoint, that of chemical warfare. I make no apology for the choice as a Presidential Address of what at first seems a highly specialized matter, for it will, I hope, become apparent that the focus of all such researches is one common to Medicine in its widest sense. Resolution of the problem will bring the answer to many difficulties, too often regarded as practical in contra-distinction to academic, an attitude I hold to be quite wrong.

When a highly irritant liquid such as lewisite or mustard gas is dropped on the skin in minute droplets, a blister forms in a few hours. The nature of this familiar disturbance is well known. It consists in the partial or complete separation of the avascular epidermis from the underlying vascular dermis by a fluid, at first free from cellular content but later fairly rich in white blood corpuscles. This fluid invariably contains other components of the blood, especially proteins and various salts. Sometimes the protein is in large amounts and may even approach a concentration of 6%, which means that the fluid is almost pure plasma from the circulating blood. The distribution of salts can be shown to obey the predictions which follow from a Gibbs-Donnan equilibrium and as such can be dismissed from this discussion without further comment. The epidermal covering or dome of the blister is so vitiated by the action of the causative agent and no doubt, too, by its separation from its nutritive bed, the dermis, that it invariably dies and later separates at the edges of attachment, thus presenting a problem to the surviving healthy structures around, a problem which is solved in the process we call regeneration. Two important features characterize the formation of such a blister, (1) the localized outpouring of blood plasma from the blood-vessels of the affected part, and (2) the detachment of the epidermis by this rush outwards of plasma. We know a good deal about the first mechanism, but very little about the second, although the important researches of Peters and his colleagues, and of Medawar, hold out promise of a solution in the discovery of proteolytic enzymes liberated after skin damage which may be responsible for loosening of the basement membrane which anchors the epidermis to the dermis.

Experimental pathology has long known that outpouring of a fluid follows injury by various means of blood-vessels, especially capillaries. There is an impressive

Section of Urology

CONTENTS

PAGE Section Volume

November 28, 1946

SOME PROBLEMS OF RENAL LITHIASIS
President's Address by R. H. O. B. Robinson, F.R.C.S. 1 201

January 23, 1947

List of Cases and Specimens shown 19 433

February 27, 1947

DISCUSSION ON THE USE OF PENICILLIN IN UROLOGY 19–28 433–442
Dr. A. L. P. Peeney 19 433
Lady Florey 26 440
Mr. Clifford Morson, Mr. Yates Bell 27 441
Mr. Edgar Freshman, Mr. Hugh Donovan 28 442

March 27, 1947

INJURIES TO THE BLADDER
Richard A. Mogg, F.R.C.S. 29 795
INJURIES OF THE URETHRA. [*Abridged*]
D. S. Poole-Wilson, F.R.C.S. 32 798
SOME OBSERVATIONS ON A PERSONAL SERIES OF BATTLE CASUALTIES INVOLVING THE GENITO-URINARY SYSTEM. [*Abridged*]
Geoffrey E. Parker, F.R.C.S. 38 804

April 24, 1947

TREATMENT OF HYDRONEPHROSIS ASSOCIATED WITH ABNORMAL VESSELS
H. Hamilton Stewart, F.R.C.S. 41 807

May 22, 1947

CLINICO-PATHOLOGICAL MEETING HELD AT ST. THOMAS'S HOSPITAL, LONDON, S.E.1

List of Cases and Specimens shown 43 809

June 26, 1947

List of Cases and Specimens shown 43 809
SURVIVAL OF A TESTICLE TRANSPLANTED INTO SCARPA'S TRIANGLE
R. Ogier Ward, D.S.O., M.Ch... .. .. 44 810

The Society does not hold itself in any way responsible for the statements made or the views put forward in the various papers.

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.

may last several days, but as lewisite not uncommonly damages red corpuscles, leading to hæmolysis, and mustard gas has a direct injurious action on the bone-marrow, it would at first seem likely that the anæmia is a toxic one. I shall present evidence later on that other factors are also concerned.

If we turn to another chemical warfare agent, phosgene, this time an irritating gas which exerts its effects only after inhalation, we find that much the same sort of changes are induced in the tissues with which the phosgene comes into contact. There is a tremendous outpouring of fluid, rich in plasma proteins, into the voluminous air spaces of the lungs and this presents a serious problem to the organism in the form of pulmonary œdema. Only too frequently is it unsolved and acute mechanical anoxia develops with death from respiratory failure. Existing evidence shows that phosgene as such is not absorbed into the blood from the air spaces so that it does not contribute to the problem through its inherent chemical properties. Lewisite and mustard gas, on the other hand, as we were able to show, can be absorbed and lead to serious systemic complications. Accompanying the pulmonary œdema of phosgene inhalation is a series of changes in the blood pattern. One cannot fail to be impressed by the similarity of this pattern with that which develops after skin application of lewisite or mustard gas. Here again is a profound depletion of the circulating plasma without any noteworthy alteration of the total cell mass. In an animal with a large splenic reservoir, the goat for instance, there is often a temporary increase of the blood cell mass as might be predicted from the Barcroft theory of splenic function, and it has been shown, by American workers, that this phenomenon does not occur in the splenectomized subject. The plasma protein concentration also falls in amounts approximately balanced by the gain of protein in the lung œdema fluid as time goes on, whilst the behaviour of the hæmoglobin percentage, red cell count and hæmatocrit percentage likewise points to concentration of the blood. In other words, there is an exact parallel in the two types of conditions. In both much plasma leaves the vessels of the affected regions and there follows hæmoconcentration from loss of this blood plasma with its consequent disturbances of circulatory function, nitrogen metabolism and the rest. Other irritant gases, including inhaled lewisite and mustard vapour and certain of the smokes, give the same kind of pattern and it is obvious that we are dealing with a series of widely differing procedures which nevertheless have a common factor.

If we now turn to a completely different process, thermal burning, we meet with much the same set of disturbances once again. Thermal burns affecting an extensive skin area give a blood pattern which differs from that described with the gases only in the rapidity of its development. Here we see an extraordinary outpouring of fluid from the blood, almost a gush of fluid, in the first half-hour after burning. This fluid is the basis of the blistering and œdema of the burnt area. It is rich in protein and in fact may be pure plasma, as chemical analysis of the burn and blister fluid shows. Again we have the familiar sequence in the blood volume change, and there is also a sharp, though usually transient, rise in the non-protein nitrogen of the blood and often a mild or fairly severe anæmia. Surely we are face to face with the same kind of circulatory upset as in the previous examples.

Finally, there are some experiments which I believe have their value in our search for the meaning of these common phenomena. If large amounts of a hypertonic solution of glucose or saline be introduced into the subcutaneous tissues of a limb of a rabbit or goat, there follows quite rapidly a severe localized œdema due to much fluid leaving the circulation. Concentration of the circulating blood follows, as shown by the rising hæmoglobin percentage and red cell count and fall of the plasma volume, whilst the familiar non-protein nitrogen increase in the blood occurs at some stage or other and persists for a short time, and there is usually a secondary anæmia. In other words, the simple abstraction of fluid from the circulation gives us the line of simple experiments commencing with the observations of British workers in the early nineteenth century, and including the famous contributions of Augustus Waller, William Addison, Thomas Wharton Jones and Lister, culminating in the classical work of Cohnheim, Starling and Lewis; all such studies show how intense and rapid, yet ordered, is the local response of blood-vessels to injury. If further proof of the importance of this fluid loss is wanted we need only consider the systemic circulatory upset consequent upon a severe involvement of a richly vascular skin in injury. When a few milligrams of lewisite or mustard gas are allowed to soak into the surface tissues of an experimental animal there soon follows a series of changes in the circulating blood which are discussed below. It is not at all difficult to estimate with considerable accuracy the fluid portion of the whole blood by modern photometric methods, based on the principle long ago established by Whipple that minute amounts of dye when allowed to mix thoroughly with the blood give a measure of the fluid in which the dye is suspended, provided little of the dye escapes from that fluid. Certain high molecular dyes are known, such as trypan blue and its isomer T.1824, which form large colloidal complexes with the plasma proteins, especially the albumin fraction, and consequently leave the circulation rather slowly. The art of this method of calculating the blood volume lies in choosing a time after the dye has been injected into the vessels, short enough to exclude much loss of the dye, yet long enough to be sure that the dye has been uniformly distributed throughout the circulating blood and intimately mixed with its plasma. With certain precautions, the modern methods give uniform results and can be used for repeated estimations of the plasma volume over a short interval of time. After the skin application of these irritants there is found a regular decline in the plasma volume, sometimes to low levels, and this depression may last two or three days. The animal may die at this stage in a condition we called lewisite or mustard-gas "shock", a state in which the animal is cold and clammy, looks ill and is difficult to bleed because its veins are collapsed and its arterial blood-pressure is low. In not so severe cases, recovery follows in gradual fashion and in five to seven days there is great improvement in the clinical condition, whilst the plasma volume has once more returned to the normal level. Associated with these changes in the fluid portion of the blood are several other striking features. It can be shown that the hæmoglobin percentage, red cell count and packed cell volume (hæmatocrit percentage) rise during the period of plasma volume decline and at the height of the "shock" indicate a severe degree of concentration of the blood. Nevertheless, suitable calculations make it clear that there is really very little alteration in the total cell mass of the circulating blood. It thus appears that though the total blood volume has greatly decreased, this is wholly because of loss of its fluid portion. The same mass of red corpuscles is still in circulation but the blood is "thickened" through depletion of its watery phase. By careful weighings and chemical analyses of the tissues through which the lewisite or mustard gas has seeped, my colleague F. C. Courtice showed that most of this lost fluid could be accounted for as œdema fluid in the gas-contaminated regions.

Protein, too, leaves the circulation with the water. The total plasma proteins fall steadily for the first two to three days after lewisite application; at the same time a protein-containing fluid can be demonstrated in the region of lewisite action. A similar state of affairs arises after mustard-gas application. We are justified, therefore, in believing that because of some action of these irritants, large amounts of plasma are induced to leave the blood-vessels, especially the capillaries, and accumulate in the zone of influence of the irritants concerned.

During the period of "shock" with decreased plasma volume and plasma proteins, the blood urea level almost invariably rises but returns rapidly to normal when the blood volume recovers. This suggests a functional rather than a pathological disturbance of the kidney (Courtice). A mild degree of secondary anæmia is often found and many fields of biology. You will remember that Starling investigated the factors underlying absorption of fluids of varying tonicity from the body cavities and spaces and, in his own words, suggested that "there must be a balance between the hydrostatic pressure of the blood in the capillaries and the osmotic attraction of the blood for the surrounding fluids". When the capillary pressure increases there is increased transudation until equilibrium is established; with lessened capillary pressure there is predominant osmotic absorption of salt solution from the extravascular fluid until this becomes richer in proteins and the difference between its protein osmotic pressure and that of the intravascular plasma is equal to the diminished capillary pressure. The capillary wall thus acts as an inert filtration membrane, the motive force for fluid exchange being the hydrostatic pressure afforded by the blood-pressure and the osmotic pressure of the proteins in the plasma and tissue fluid. Starling was also aware that the tissues could exert a mechanical pressure, much less, it is true, than that exerted by the capillaries, and he actually measured this on many occasions. Such tissue pressure would oppose the force which presses fluid from the vessels. This balanced set of forces thus allows of the passage of water and crystalloids to and fro between the capillaries and the tissue spaces. Protein, however, requires another mechanism for absorption and this, Starling thought, resides in the lymphatics.

Fifty years of experimentation has done little to upset the Starling theory; indeed, more and more data have accumulated in support of what must be regarded as one of the great generalizations of physiology. The relative constancy of blood volume and tissue fluid volume has been established many times and technical improvements in measuring capillary pressure, osmotic pressure of plasma proteins, lymph flow and composition and tissue pressure have given results which are in remarkable agreement with the postulates of the theory. The capillary bed of the organism thus becomes a gigantic filtering surface, estimated by Krogh as being somewhat greater than 6,300 square metres in man, or as Landis so vividly puts it, equal to a minutely thin membrane three feet wide and four miles in length. Such a surface is ideal for rapid interchange of fluid. Over it drifts the blood at a pressure of 22 to 45 cm. water which tends to force plasma through the membrane. The fluid portion of the blood contains various protein fractions, for convenience labelled albumins and globulins, which exert an osmotic force of about 36 cm. water and this force attracts fluid through the filter bed into the main channel of flow. But the bed is of variable extent and its fluctuations lead to variation in filtering pressure and fluid flow. When the capillaries widen, as for example after warming, more fluid passes over the surface, the hydrostatic pressure increases, and filtration is enhanced. Hence more filtrate leaves the vessels for the tissues and œdema results. It must be emphasized that the filter has the important property of allowing only very small amounts of protein to pass through so that on one side it encloses water, crystalloids and very large molecules of protein, on the other side it is in contact with a salt solution containing very small amounts of protein. In this way there is maintained an additional motive force (the osmotic pressure) inherent in the large molecules within the capillaries. Despite this osmotic pressure being quite small in comparison with that of the crystalloids, it is an effective one, acting as it does almost unopposed, and being of a dimension not far removed from the hydrostatic pressure.

A little thought convinces one that the filter membrane plays a highly important part in equilibrium maintenance. At least 95% of the circulating protein is held back by the membrane in most parts of the body (Landis), though there are regions which permit a free passage of protein, notably in the liver and alimentary canal. Anything which makes the filter more leaky should, on the Starling theory, lead to great disturbance of fluid equilibrium for the proteins would pass to the tissue spaces and swing the balance of forces over to the side of attraction. In this way the counter-

complicated pattern of events we have recognized after the action of strong irritant liquids on the skin, thermal burning or inhalation of certain gases. It is not too much to suggest that many, if not all of the phenomena, follow upon the acute anhydræmia, no matter how it is induced. Further support for this view has been obtained through the careful experiments of my colleagues, F. C. Courtice and G. L. Foss, who have shown that much may be done to mitigate the serious features of gas anhydræmia by the intelligent use of plasma transfusion, whilst my assistants, J. D. Allen, R. F. G. Coles and J. P. Rutland and I have confirmed the beneficial action of plasma found by many other workers in the case of thermal burns. We also have obtained encouraging results in the treatment of the "shock" period of mustard-gas poisoning by using plasma. Of course, caution has to be exercised with this therapy for at certain stages of pulmonary œdema the administered fluid may leave the circulation for the lungs and add to the load of exudate already carried by the air spaces.

It would be wrong to leave this part of the story without referring to some of the compensatory mechanisms the anhydræmic organism calls into play when the crisis is precipitated. Perhaps the most important of these is the mobilization of fluid and protein from all available depots in the body, in an attempt to restore the depleted blood or rather plasma volume. The necessity for such emergency measures is of course shown by the grave results of continued anhydræmia, evidenced by the falling blood-pressure in the arteries and veins, the decline in body temperature—surely a manifestation of depressed metabolism—and the signs of functional upset in certain organs, especially the kidneys. That fluid is withdrawn from many sources is plainly shown by the dehydrated condition of many tissues, whilst the thirst the animal exhibits also suggests an urgent call for fluid from without. We have some reason to believe that fluid within the alimentary canal may also be drawn upon in this hour of need. Compensation for protein deficiency is indicated in the lag shown by the falling plasma protein curve which is a striking feature of all our examples, and indeed there may be postponement of the fall in protein concentration for a considerable period of time. This indicates that protein depots readily give up their labile reserves of protein (Whipple) and indeed they may be prepared to offer even more valuable gifts of protein from their resources.

In addition, there is evidence that some at least of the lost fluid and protein is returned to the circulation by way of the lymphatics which drain the sites involved in the fluid loss. We are familiar with the idea of increased lymph flow from burnt areas through the beautiful researches of Drinker and his associates. Courtice has employed similar methods in our own studies and has cannulated the lymphatics of limbs and even of the lungs in animals contaminated with poison gases. With truly remarkable skill he has followed the course of lymph flow for many hours after these injuries, and has given us convincing evidence that such flow is increased, both of water and protein. That such protein-rich lymph is added to the circulation is shown by the increase in thoracic duct flow at the period of greatest fluid loss from the blood-stream. Clearly, this form of compensation is of limited value and indeed may add to the troubles of the harassed organism by introducing some of the harmful chemical into the blood-stream.

Finally, the already well-known compensatory processes of vasoconstriction and blood shift affecting the vascular territories of the less "vital" tissues no doubt play an important part, but we have nothing to contribute to this field of research. I believe that much requires to be done in this domain for here we may find the secret of the case which ends in death.

How are we to put together the facts so briefly outlined in the above description? Exactly fifty years ago, the great physiologist, E. H. Starling, propounded his theory of fluid balance between the tissues and blood which has proved so illuminating in

many fields of biology. You will remember that Starling investigated the factors underlying absorption of fluids of varying tonicity from the body cavities and spaces and, in his own words, suggested that "there must be a balance between the hydrostatic pressure of the blood in the capillaries and the osmotic attraction of the blood for the surrounding fluids". When the capillary pressure increases there is increased transudation until equilibrium is established: with lessened capillary pressure there is predominant osmotic absorption of salt solution from the extravascular fluid until this becomes richer in proteins and the difference between its protein osmotic pressure and that of the intravascular plasma is equal to the diminished capillary pressure. The capillary wall thus acts as an inert filtration membrane, the motive force for fluid exchange being the hydrostatic pressure afforded by the blood-pressure and the osmotic pressure of the proteins in the plasma and tissue fluid. Starling was also aware that the tissues could exert a mechanical pressure, much less, it is true, than that exerted by the capillaries, and he actually measured this on many occasions. Such tissue pressure would oppose the force which presses fluid from the vessels. This balanced set of forces thus allows of the passage of water and crystalloids to and fro between the capillaries and the tissue spaces. Protein, however, requires another mechanism for absorption and this, Starling thought, resides in the lymphatics.

Fifty years of experimentation has done little to upset the Starling theory; indeed, more and more data have accumulated in support of what must be regarded as one of the great generalizations of physiology. The relative constancy of blood volume and tissue fluid volume has been established many times and technical improvements in measuring capillary pressure, osmotic pressure of plasma proteins, lymph flow and composition and tissue pressure have given results which are in remarkable agreement with the postulates of the theory. The capillary bed of the organism thus becomes a gigantic filtering surface, estimated by Krogh as being somewhat greater than 6,300 square metres in man, or as Landis so vividly puts it, equal to a minutely thin membrane three feet wide and four miles in length. Such a surface is ideal for rapid interchange of fluid. Over it drifts the blood at a pressure of 22 to 45 cm. water which tends to force plasma through the membrane. The fluid portion of the blood contains various protein fractions, for convenience labelled albumins and globulins, which exert an osmotic force of about 36 cm. water and this force attracts fluid through the filter bed into the main channel of flow. But the bed is of variable extent and its fluctuations lead to variation in filtering pressure and fluid flow. When the capillaries widen, as for example after warming, more fluid passes over the surface, the hydrostatic pressure increases, and filtration is enhanced. Hence more filtrate leaves the vessels for the tissues and œdema results. It must be emphasized that the filter has the important property of allowing only very small amounts of protein to pass through so that on one side it encloses water, crystalloids and very large molecules of protein, on the other side it is in contact with a salt solution containing very small amounts of protein. In this way there is maintained an additional motive force (the osmotic pressure) inherent in the large molecules within the capillaries. Despite this osmotic pressure being quite small in comparison with that of the crystalloids, it is an effective one, acting as it does almost unopposed, and being of a dimension not far removed from the hydrostatic pressure.

A little thought convinces one that the filter membrane plays a highly important part in equilibrium maintenance. At least 95% of the circulating protein is held back by the membrane in most parts of the body (Landis), though there are regions which permit a free passage of protein, notably in the liver and alimentary canal. Anything which makes the filter more leaky should, on the Starling theory, lead to great disturbance of fluid equilibrium for the proteins would pass to the tissue spaces and swing the balance of forces over to the side of attraction. In this way the counter-

complicated pattern of events we have recognized after the action of strong irritant liquids on the skin, thermal burning or inhalation of certain gases. It is not too much to suggest that many, if not all of the phenomena, follow upon the acute anhydræmia, no matter how it is induced. Further support for this view has been obtained through the careful experiments of my colleagues, F. C. Courtice and G. L. Foss, who have shown that much may be done to mitigate the serious features of gas anhydræmia by the intelligent use of plasma transfusion, whilst my assistants, J. D. Allen, R. F. G. Coles and J. P. Rutland and I have confirmed the beneficial action of plasma found by many other workers in the case of thermal burns. We also have obtained encouraging results in the treatment of the "shock" period of mustard-gas poisoning by using plasma. Of course, caution has to be exercised with this therapy for at certain stages of pulmonary œdema the administered fluid may leave the circulation for the lungs and add to the load of exudate already carried by the air spaces.

It would be wrong to leave this part of the story without referring to some of the compensatory mechanisms the anhydræmic organism calls into play when the crisis is precipitated. Perhaps the most important of these is the mobilization of fluid and protein from all available depots in the body, in an attempt to restore the depleted blood or rather plasma volume. The necessity for such emergency measures is of course shown by the grave results of continued anhydræmia, evidenced by the falling blood-pressure in the arteries and veins, the decline in body temperature—surely a manifestation of depressed metabolism—and the signs of functional upset in certain organs, especially the kidneys. That fluid is withdrawn from many sources is plainly shown by the dehydrated condition of many tissues, whilst the thirst the animal exhibits also suggests an urgent call for fluid from without. We have some reason to believe that fluid within the alimentary canal may also be drawn upon in this hour of need. Compensation for protein deficiency is indicated in the lag shown by the falling plasma protein curve which is a striking feature of all our examples, and indeed there may be postponement of the fall in protein concentration for a considerable period of time. This indicates that protein depots readily give up their labile reserves of protein (Whipple) and indeed they may be prepared to offer even more valuable gifts of protein from their resources.

In addition, there is evidence that some at least of the lost fluid and protein is returned to the circulation by way of the lymphatics which drain the sites involved in the fluid loss. We are familiar with the idea of increased lymph flow from burnt areas through the beautiful researches of Drinker and his associates. Courtice has employed similar methods in our own studies and has cannulated the lymphatics of limbs and even of the lungs in animals contaminated with poison gases. With truly remarkable skill he has followed the course of lymph flow for many hours after these injuries, and has given us convincing evidence that such flow is increased, both of water and protein. That such protein-rich lymph is added to the circulation is shown by the increase in thoracic duct flow at the period of greatest fluid loss from the blood-stream. Clearly, this form of compensation is of limited value and indeed may add to the troubles of the harassed organism by introducing some of the harmful chemical into the blood-stream.

Finally, the already well-known compensatory processes of vasoconstriction and blood shift affecting the vascular territories of the less "vital" tissues no doubt play an important part, but we have nothing to contribute to this field of research. I believe that much requires to be done in this domain for here we may find the secret of the case which ends in death.

How are we to put together the facts so briefly outlined in the above description? Exactly fifty years ago, the great physiologist, E. H. Starling, propounded his theory of fluid balance between the tissues and blood which has proved so illuminating in

many fields of biology. You will remember that Starling investigated the factors underlying absorption of fluids of varying tonicity from the body cavities and spaces and, in his own words, suggested that "there must be a balance between the hydrostatic pressure of the blood in the capillaries and the osmotic attraction of the blood for the surrounding fluids". When the capillary pressure increases there is increased transudation until equilibrium is established: with lessened capillary pressure there is predominant osmotic absorption of salt solution from the extravascular fluid until this becomes richer in proteins and the difference between its protein osmotic pressure and that of the intravascular plasma is equal to the diminished capillary pressure. The capillary wall thus acts as an inert filtration membrane, the motive force for fluid exchange being the hydrostatic pressure afforded by the blood-pressure and the osmotic pressure of the proteins in the plasma and tissue fluid. Starling was also aware that the tissues could exert a mechanical pressure, much less, it is true, than that exerted by the capillaries, and he actually measured this on many occasions. Such tissue pressure would oppose the force which presses fluid from the vessels. This balanced set of forces thus allows of the passage of water and crystalloids to and fro between the capillaries and the tissue spaces. Protein, however, requires another mechanism for absorption and this, Starling thought, resides in the lymphatics.

Fifty years of experimentation has done little to upset the Starling theory; indeed, more and more data have accumulated in support of what must be regarded as one of the great generalizations of physiology. The relative constancy of blood volume and tissue fluid volume has been established many times and technical improvements in measuring capillary pressure, osmotic pressure of plasma proteins, lymph flow and composition and tissue pressure have given results which are in remarkable agreement with the postulates of the theory. The capillary bed of the organism thus becomes a gigantic filtering surface, estimated by Krogh as being somewhat greater than 6,300 square metres in man, or as Landis so vividly puts it, equal to a minutely thin membrane three feet wide and four miles in length. Such a surface is ideal for rapid interchange of fluid. Over it drifts the blood at a pressure of 22 to 45 cm. water which tends to force plasma through the membrane. The fluid portion of the blood contains various protein fractions, for convenience labelled albumins and globulins, which exert an osmotic force of about 36 cm. water and this force attracts fluid through the filter bed into the main channel of flow. But the bed is of variable extent and its fluctuations lead to variation in filtering pressure and fluid flow. When the capillaries widen, as for example after warming, more fluid passes over the surface, the hydrostatic pressure increases, and filtration is enhanced. Hence more filtrate leaves the vessels for the tissues and œdema results. It must be emphasized that the filter has the important property of allowing only very small amounts of protein to pass through so that on one side it encloses water, crystalloids and very large molecules of protein, on the other side it is in contact with a salt solution containing very small amounts of protein. In this way there is maintained an additional motive force (the osmotic pressure) inherent in the large molecules within the capillaries. Despite this osmotic pressure being quite small in comparison with that of the crystalloids, it is an effective one, acting as it does almost unopposed, and being of a dimension not far removed from the hydrostatic pressure.

A little thought convinces one that the filter membrane plays a highly important part in equilibrium maintenance. At least 95% of the circulating protein is held back by the membrane in most parts of the body (Landis), though there are regions which permit a free passage of protein, notably in the liver and alimentary canal. Anything which makes the filter more leaky should, on the Starling theory, lead to great disturbance of fluid equilibrium for the proteins would pass to the tissue spaces and swing the balance of forces over to the side of attraction. In this way the counter-

complicated pattern of events we have recognized after the action of strong irritant liquids on the skin, thermal burning or inhalation of certain gases. It is not too much to suggest that many, if not all of the phenomena, follow upon the acute anhydræmia, no matter how it is induced. Further support for this view has been obtained through the careful experiments of my colleagues, F. C. Courtice and G. L. Foss, who have shown that much may be done to mitigate the serious features of gas anhydræmia by the intelligent use of plasma transfusion, whilst my assistants, J. D. Allen, R. F. G. Coles and J. P. Rutland and I have confirmed the beneficial action of plasma found by many other workers in the case of thermal burns. We also have obtained encouraging results in the treatment of the "shock" period of mustard-gas poisoning by using plasma. Of course, caution has to be exercised with this therapy for at certain stages of pulmonary œdema the administered fluid may leave the circulation for the lungs and add to the load of exudate already carried by the air spaces.

It would be wrong to leave this part of the story without referring to some of the compensatory mechanisms the anhydræmic organism calls into play when the crisis is precipitated. Perhaps the most important of these is the mobilization of fluid and protein from all available depots in the body, in an attempt to restore the depleted blood or rather plasma volume. The necessity for such emergency measures is of course shown by the grave results of continued anhydræmia, evidenced by the falling blood-pressure in the arteries and veins, the decline in body temperature—surely a manifestation of depressed metabolism—and the signs of functional upset in certain organs, especially the kidneys. That fluid is withdrawn from many sources is plainly shown by the dehydrated condition of many tissues, whilst the thirst the animal exhibits also suggests an urgent call for fluid from without. We have some reason to believe that fluid within the alimentary canal may also be drawn upon in this hour of need. Compensation for protein deficiency is indicated in the lag shown by the falling plasma protein curve which is a striking feature of all our examples, and indeed there may be postponement of the fall in protein concentration for a considerable period of time. This indicates that protein depots readily give up their labile reserves of protein (Whipple) and indeed they may be prepared to offer even more valuable gifts of protein from their resources.

In addition, there is evidence that some at least of the lost fluid and protein is returned to the circulation by way of the lymphatics which drain the sites involved in the fluid loss. We are familiar with the idea of increased lymph flow from burnt areas through the beautiful researches of Drinker and his associates. Courtice has employed similar methods in our own studies and has cannulated the lymphatics of limbs and even of the lungs in animals contaminated with poison gases. With truly remarkable skill he has followed the course of lymph flow for many hours after these injuries, and has given us convincing evidence that such flow is increased, both of water and protein. That such protein-rich lymph is added to the circulation is shown by the increase in thoracic duct flow at the period of greatest fluid loss from the blood-stream. Clearly, this form of compensation is of limited value and indeed may add to the troubles of the harassed organism by introducing some of the harmful chemical into the blood-stream.

Finally, the already well-known compensatory processes of vasoconstriction and blood shift affecting the vascular territories of the less "vital" tissues no doubt play an important part, but we have nothing to contribute to this field of research. I believe that much requires to be done in this domain for here we may find the secret of the case which ends in death.

How are we to put together the facts so briefly outlined in the above description? Exactly fifty years ago, the great physiologist, E. H. Starling, propounded his theory of fluid balance between the tissues and blood which has proved so illuminating in

Sectional page 1 *Proceedings of the Royal Society of Medicine* Vol. XL 7

Section of Dermatology

President—Sydney Thomson, M.D.

[*October 17, 1946*]

Case for Diagnosis. ? Lichen Planus Hypertrophicus.—C. H. Whittle, M.D.

D. U., Corporal in the R.A.F., aged 24.

Four years' history of somewhat itchy nodules on front of shins, first appearing when he was in Rhodesia. These have been getting larger and more numerous. The largest lesions are oval about 2 in. long and 1½ in. in diameter, the long axis along the length of the shin : they are bluish-red warty nodes raised ¼ in. or more above the surface, with numerous keratin plugs in the follicles : there are smaller earlier outlying lesions. There is a similar bluish-red scaly plaque at the root of the penis ¾ in. in diameter.

Biopsy.—The sections show warty hyperplasia and hyperkeratosis of the epidermis and there is a fairly dense mixed cellular exudate in the corium, with some œdema. Stains for amyloid and for mucin show neither of these changes.

Wassermann reaction negative.

17.10.46: There are now some lichen planus papules on the wrists. He is shown because of the resistance to treatment of the warty lesions on the legs in such cases. Large doses of vitamin A are now being given, and results will be reported.

2.12.46: No change. C. H. W.

Hæmorrhagic Telangiectasia of Rendu-Osler-Weber, with No Family History.—C. H. Whittle, M.D.

D. L., an undergraduate, aged 23.

Seven years' history of persistent bluish-red macules on the backs of the hands; no symptoms. Also occasional nose-bleeds in same period.

The lesions are 1 mm. to 1 cm. in diameter and I think are made up of a network of fine blood-vessels. They are more noticeable in hot weather.

Family history.—His mother is a doctor; there is no traceable family history of a like condition. (*Note:* Pulmonary tuberculosis was diagnosed a year ago by mass radiography: symptomless, and no cough or sputum.)

Diagnosis.—This might be regarded as a case of vascular nævi, plus nose-bleeds, but I would prefer the diagnosis given. Another alternative is telangiectasia macularis eruptiva perstans, but the lesions are very few, limited to the hands, and unlike in this respect any of the other cases hitherto described (Weber, F. Parkes, Barber, H. W., Fox, Colcott *et al.*) There seem to be a few cases of true hæmorrhagic telangiectasia without any hereditary factor traceable, e.g. Whittle, C. H. (1945), *Brit. J. Derm.*, 57, 157.

Stock (1944, *Arch. Otolaryng.*, 40, 108-114), in a comprehensive review of the literature, concludes that "it is highly probable that in about 20% of the recorded cases the disease developed in the total absence of a family history of its occurrence. Whether the patients in these cases can transmit the disease to their progeny is not known".

Hæmorrhagic Telangiectasia of Rendu-Osler-Weber.—C. H. Whittle, M.D.

E. B., a married woman, aged 60.

Twenty years' history of bluish-red spots on tongue. Fifteen years' history of attacks of nose-bleeding. No hæmatemesis or melæna reported; no hæmaturia.

balance to hydrostatic pressure would be lessened and filtration would go on unrestricted until equilibrium was again asserted.

I believe that this is the basis of what was going on in the experiments I have described with irritants and burning. The rapid appearance in the tissues of a fluid rich in protein certainly suggests that the filter had let through these large molecules in a quite unusual fashion. My colleague, R. H. D. Short, was able to show that at a very early period after the application of lewisite or mustard gas to the skin, the capillaries became more permeable to a dye such as T.1824. Now this dye combines in some sort of way with the plasma albumin, as Ogston found out for us by means of ultra-centrifugation, so it is plain that capillary permeability had changed. Even after five minutes such an increase has been demonstrated by Short and by our colleagues, H. Cullumbine and H. N. Rydon, both in man and in animals. A similar disturbance can be shown to be at work in the lungs affected by irritant gases and smokes, though here we have to keep in mind an additional factor in the form of anoxia. These irritant gases frequently if not always induce early bronchial constriction which if continued leads on to anoxia. We owe to Landis and Drinker many reasons for believing that anoxia increases the permeability of capillaries; Landis, for instance, has shown that the minute vessels in the frog's mesentery may become three times as permeable in the presence of anoxæmia.

Whatever may be the factors concerned, the central point of our investigations is, I am firmly convinced, alteration of capillary permeability through the action of the gases, &c., on the tissues. We are faced with the greatest of all problems in pathology once more.

Cullumbine and Rydon demonstrated the production of Menkin's leukotaxin in tissues damaged by mustard gas, and this compound, together with the histamine-like substances of Lewis, is no doubt the intermediary in bringing about the capillary wall change which underlies increased permeability for plasma proteins. Once this view is accepted, most of the phenomena I have described follow in due course and the common story becomes an intelligible one.

But what of this fundamental permeability change which receives emphasis again and again in physiology and pathology? Is it a physical or chemical alteration in the surface membrane of the lining endothelial cells of the vessels, or can it be attributed to a loosening of the cement substance which binds together these cells, as was suggested originally by Sidney Ringer and again in recent years by Robert Chambers and his school? Are living processes concerned, bound up with the life of cells or must we look to the biophysicist for the answer?

The remarkable studies of Peters and Dixon on enzyme chemistry and chemical warfare agents have opened up a new way of approach to the permeability problem which may bring the solution, but are we to wait for the outbreak of fresh horrors of man's ingenuity to enable an organized and adequate attack on this most vital of problems?

BIBLIOGRAPHY

I have drawn freely on a series of reports prepared by colleagues and myself, working at the Chemical Defence Experimental Station, Porton, for the Ministry of Supply during the 1939-45 war years. Some of these reports are in process of publication. In addition, I have made use of the following papers :—

CAMERON, G. R. (1945) *Brit. Med. Bull.*, 3, 88.
——, ALLEN, J. W., COLES, R. F. G., and RUTLAND, J. P. (1945) *J. Path. Bact.*, 57, 37.
COURTICE, F. C. (1946) *J. Physiol.*, 104, 321.
CULLUMBINE, H., and RYDON, H. N. (1946) *Brit. J. exp. Path.*, 27, 33.
DRINKER, C. K., and FIELD, M. E. (1933) Lymphatics, Lymph and Tissue Fluid. Baltimore.
——, and YOFFEY, J. M. (1941) Lymphatics, Lymph and Lymphoid Tissue. Harvard University Press, Cambridge, Mass.
LANDIS, E. M. (1937) *Amer. J. med. Sci.*, 193, 297.
LEACH, E. H., PETERS, R. A., and ROSSITER, R. J. (1943) *Quart. J. exp. Physiol.*, 32, 67.
MEDAWAR, P. B. (1941) *Nature*, 148, 783.
STARLING, E. H. (1895-6) *J. Physiol.*, 19, 312.
PETERS, J. P. (1945) *Physiol. Rev.*, 25, 491.

Section of Dermatology

President—SYDNEY THOMSON, M.D.

[*October* 17, 1946]

Case for Diagnosis. ? Lichen Planus Hypertrophicus.—C. H. WHITTLE, M.D.

D. U., Corporal in the R.A.F., aged 24.

Four years' history of somewhat itchy nodules on front of shins, first appearing when he was in Rhodesia. These have been getting larger and more numerous. The largest lesions are oval about 2 in. long and 1½ in. in diameter, the long axis along the length of the shin: they are bluish-red warty nodes raised ¼ in. or more above the surface, with numerous keratin plugs in the follicles: there are smaller earlier outlying lesions. There is a similar bluish-red scaly plaque at the root of the penis ¼ in. in diameter.

Biopsy.—The sections show warty hyperplasia and hyperkeratosis of the epidermis and there is a fairly dense mixed cellular exudate in the corium, with some œdema. Stains for amyloid and for mucin show neither of these changes.

Wassermann reaction negative.

17.10.46: There are now some lichen planus papules on the wrists. He is shown because of the resistance to treatment of the warty lesions on the legs in such cases. Large doses of vitamin A are now being given, and results will be reported.

2.12.46: No change. C. H. W.

Hæmorrhagic Telangiectasia of Rendu-Osler-Weber, with No Family History.—C. H. WHITTLE, M.D.

D. L., an undergraduate, aged 23.

Seven years' history of persistent bluish-red macules on the backs of the hands; no symptoms. Also occasional nose-bleeds in same period.

The lesions are 1 mm. to 1 cm. in diameter and I think are made up of a network of fine blood-vessels. They are more noticeable in hot weather.

Family history.—His mother is a doctor; there is no traceable family history of a like condition. (*Note:* Pulmonary tuberculosis was diagnosed a year ago by mass radiography: symptomless, and no cough or sputum.)

Diagnosis.—This might be regarded as a case of vascular nævi, plus nose-bleeds, but I would prefer the diagnosis given. Another alternative is telangiectasia macularis eruptiva perstans, but the lesions are very few, limited to the hands, and unlike in this respect any of the other cases hitherto described (Weber, F. Parkes, Barber, H. W., Fox, Colcott *et al.*) There seem to be a few cases of true hæmorrhagic telangiectasia without any hereditary factor traceable, e.g. Whittle, C. H. (1945), *Brit. J. Derm.*, 57, 157.

Stock (1944, *Arch. Otolaryng.*, 40, 108-114), in a comprehensive review of the literature, concludes that "it is highly probable that in about 20% of the recorded cases the disease developed in the total absence of a family history of its occurrence. Whether the patients in these cases can transmit the disease to their progeny is not known".

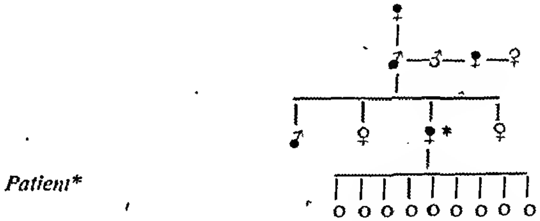
Hæmorrhagic Telangiectasia of Rendu-Osler-Weber.—C. H. WHITTLE, M.D.

E. B., a married woman, aged 60.

Twenty years' history of bluish-red spots on tongue. Fifteen years' history of attacks of nose-bleeding. No hæmatemesis or melæna reported; no hæmaturia.

Recently there arose a tendency for spots on tongue to bleed, and these led to her seeking advice. There were several telangiectatic spots on the sides and front of tongue, but I have electro-cauterized most of them. There are still spots on right thumb, left little finger and on the palate up to 6 mm. diameter, which tend to bleed into the skin.

Family history.—Paternal grandmother—"nosebleeds and spots"; father—was bleeder—died of hæmatemesis aged 46; father's sister—nose-bleeds; patient's brother—nose-bleeds and cerebral hæmorrhage. Patient's nine children so far unaffected, cf. Weber, F. Parkes (1939) *Brit. J. Derm.*, **51**, 468; (1938) *Brit. J. Derm.*, **50**, 94. Wigley, J. E. M., and Heggs, Gordon (1935) *Brit. J. Derm.*, **47**, 125.



FAMILY TREE. *Black indicates those affected.*

Darier's Disease and Generalized Pruritus.—LOUIS FORMAN, M.D.

H. B., aged 63, house painter. Has had many attacks of colic.

Fifteen years ago he had a perforated duodenal ulcer. Eight years ago, short attack of generalized pruritus.

He has noticed rough papules on the neck and groins for many years, and has complained of pruritus over the chest, axillæ and groins for two years.

On admission to hospital, there were excoriations over the trunk and horny papules on both sides of the neck, forearms, lower abdomen, hips, groins, and on skin near the anus. Some of the papules had been excoriated by scratching. A moist, raised plaque developed in the groin while he was in hospital.

Biopsy showed the characteristic changes of Darier's disease in a papule from the hip and in the plaque in the groin.

The treatment given was injections of testosterone, 20 mg. every other day for five weeks, with improvement of the pruritus.

Darier's disease is an inherited dysplasia of a nævoid character and as such may well be affected by endocrine changes. This may explain the development of the moist plaque during the administration of the testosterone.

Case for Diagnosis. ? Lichen Sclerosus.—H. J. WALLACE, M.D.

Mrs. A. T., aged 49. The eruption is said to have begun as a group of blisters eight years ago. Since then she has had other groups of blisters in different areas of the body from time to time, particularly the lower trunk and legs.

Past and family history.—Nothing relevant.

Aggregates of blisters have been observed to come and go over a period of months, often leaving scarring. A typical area consists of dome-shaped irritable papules, bluish-red in colour, varying in diameter from one to three millimetres and with a smooth surface. Many of these papules develop vesicles some of which become pustular. Mucous membranes not affected. No evidence of organic disease elsewhere. Complete blood-count normal. Blood Wassermann reaction negative. Biopsy shows hyperkeratosis; acanthosis with chronic inflammation of dermis; mild perivascular lymphocytic infiltration. She has received treatment with Fowler's solution, sulphapyridine, a course of bismuth injections, thyroid for long periods, liquor hydrarg. perchlor. by mouth for four months, all without effect.

A tentative diagnosis has been made of bullous lichen sclerosus.

Dr. L. Forman: This patient was under my care in 1939 and again in 1941. She developed blisters and superficial ulceration, which took two or three months to heal. Section of a group of thick roofed blisters on the abdomen showed thickening of the epidermis, intercellular œdema of the epidermis and the formation of blisters within the epidermis. Potassium iodide 5 grains (0·3 G.) t.d.s. was given for a week, and two new areas appeared on the right leg and ankle. They were circinate, erythematous patches with thick-roofed vesicles. 30% iodide ointment was applied to healed areas and small blisters appeared around the healed sites.

The diagnosis suggested was the erythema multiforme type of pemphigus.

Keratoderma Palmaris et Plantaris.—G. C. Wells, M.R.C.P. (for H. J. Wallace, M.D.).

H. L., aged 37, a labourer. This man has callosities of the palms and soles which first became painful about ten years ago. But he thinks that he has had "hard skin" on the hands and feet since childhood. He had to give up manual work six months ago because of the pain in the hands, but since then the lesions have remained unaltered.

There is nothing to suggest that he has had arsenic at any time.

Family history.—He tells us that of his four brothers and four sisters, one brother and one sister are affected. His mother and a sister of hers, and his maternal grandfather are also affected. One of his two daughters has a small lesion on one foot.

There was no consanguinity between his parents.

It is interesting to note that only the feet show the keratosis in all his affected relatives, whereas this patient has well-marked lesions of the hands as well.

There is a patchy symmetrical keratosis of the palms and soles, affecting mainly the pressure points, and there is some degree of pes cavus. Hyperidrosis is not a feature. There is not the diffuse involvement of surface that is seen in tylosis, nor are there the fine pitted lesions of punctate keratosis. While the general appearance suggests callosities, the persistence of the condition is against a simple mechanical origin.

The family history as far as it goes points to the trait being inherited as a regular Mendelian dominant. This is in keeping with previous observations on families showing keratoderma disseminatum palmaris et plantaris.

The President: I have seen one case, in a girl, but she was an unco-operative subject. At the time I tried to read up the literature, but it is very difficult to find any classification or grouping, and there seem to be very few cases published.

Lichen Nitidus.—J. R. Simpson, M.B. (for H. J. Wallace, M.D.).

Terence D., aged 9 years.

History.—The eruption was first noticed on the abdomen in March 1946. Since then there has been a steady spread to many other areas, with no evidence of resolution anywhere. There has been no itching. The mother gives no relevant past or family history. In particular there is no history of skin disease or of tuberculosis.

On examination.—The lesions are minute, wholly discrete papules, varying in size from 0·5 mm. to 2 mm. in diameter, but otherwise of uniform character. Their surfaces are glistening. Some are flat and some are dome-shaped, but all are easily palpable. There is no erythema or scaling and the colour is that of normal skin.

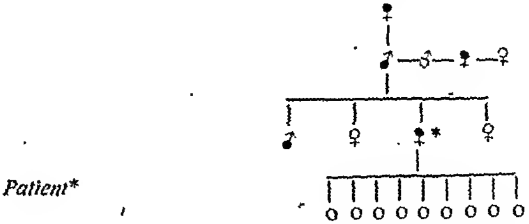
They are grouped together in colonies of varying size, distributed profusely on the trunk and limbs, and also on the penis, the forehead and right cheek. They are not related to the pilo-sebaceous follicles. The mucous membranes and the palms and soles are normal. Nothing abnormal was found on general examination.

Investigations.—X-ray of chest: No abnormality seen. Mantoux test: 1 : 10,000 negative; 1 : 1,000 negative. Biopsy from lesions on the right hypochondrium shows histological features characteristic of lichen nitidus.

Comment.—In view of the original conception that the ætiology of this condition was tuberculous he has been treated with calciferol, 100,000 i.u. daily. He has had

Recently there arose a tendency for spots on tongue to bleed, and these led to her seeking advice. There were several telangiectatic spots on the sides and front of tongue, but I have electro-cauterized most of them. There are still spots on right thumb, left little finger and on the palate up to 6 mm. diameter, which tend to bleed into the skin.

Family history.—Paternal grandmother—"nosebleeds and spots"; father—was bleeder—died of hæmatemesis aged 46; father's sister—nose-bleeds; patient's brother—nose-bleeds and cerebral hæmorrhage. Patient's nine children so far unaffected, cf. Weber, F. Parkes (1939) *Brit. J. Derm.*, **51**, 468; (1938) *Brit. J. Derm.*, **50**, 94. Wigley, J. E. M., and Heggs, Gordon (1935) *Brit. J. Derm.*, **47**, 125.



FAMILY TREE. *Black indicates those affected.*

Darier's Disease and Generalized Pruritus.—LOUIS FORMAN, M.D.

H. B., aged 63, house painter. Has had many attacks of colic.

Fifteen years ago he had a perforated duodenal ulcer. Eight years ago, short attack of generalized pruritus.

He has noticed rough papules on the neck and groins for many years, and has complained of pruritus over the chest, axillæ and groins for two years.

On admission to hospital, there were excoriations over the trunk and horny papules on both sides of the neck, forearms, lower abdomen, hips, groins, and on skin near the anus. Some of the papules had been excoriated by scratching. A moist, raised plaque developed in the groin while he was in hospital.

Biopsy showed the characteristic changes of Darier's disease in a papule from the hip and in the plaque in the groin.

The treatment given was injections of testosterone, 20 mg. every other day for five weeks, with improvement of the pruritus.

Darier's disease is an inherited dysplasia of a nævoid character and as such may well be affected by endocrine changes. This may explain the development of the moist plaque during the administration of the testosterone.

Case for Diagnosis. ? Lichen Sclerosus.—H. J. WALLACE, M.D.

Mrs. A. T., aged 49. The eruption is said to have begun as a group of blisters eight years ago. Since then she has had other groups of blisters in different areas of the body from time to time, particularly the lower trunk and legs.

Past and family history.—Nothing relevant.

Aggregates of blisters have been observed to come and go over a period of months, often leaving scarring. A typical area consists of dome-shaped irritable papules, bluish-red in colour, varying in diameter from one to three millimetres and with a smooth surface. Many of these papules develop vesicles some of which become pustular. Mucous membranes not affected. No evidence of organic disease elsewhere. Complete blood-count normal. Blood Wassermann reaction negative. Biopsy shows hyperkeratosis; acanthosis with chronic inflammation of dermis; mild perivascular lymphocytic infiltration. She has received treatment with Fowler's solution, sulphapyridine, a course of bismuth injections, thyroid for long periods, liquor hydrarg. perchlor. by mouth for four months, all without effect.

A tentative diagnosis has been made of bullous lichen sclerosus.

Dr. L. Forman: This patient was under my care in 1939 and again in 1941. She developed blisters and superficial ulceration, which took two or three months to heal. Section of a group of thick roofed blisters on the abdomen showed thickening of the epidermis, intercellular œdema of the epidermis and the formation of blisters within the epidermis. Potassium iodide 5 grains (0·3 G.) t.d.s. was given for a week, and two new areas appeared on the right leg and ankle. They were circinate, erythematous patches with thick-roofed vesicles. 30% iodide ointment was applied to healed areas and small blisters appeared around the healed sites.

The diagnosis suggested was the erythema multiforme type of pemphigus.

Keratoderma Palmaris et Plantaris.—G. C. WELLS, M.R.C.P. (for H. J. WALLACE, M.D.).

H. L., aged 37, a labourer. This man has callosities of the palms and soles which first became painful about ten years ago. But he thinks that he has had "hard skin" on the hands and feet since childhood. He had to give up manual work six months ago because of the pain in the hands, but since then the lesions have remained unaltered.

There is nothing to suggest that he has had arsenic at any time.

Family history.—He tells us that of his four brothers and four sisters, one brother and one sister are affected. His mother and a sister of hers, and his maternal grandfather are also affected. One of his two daughters has a small lesion on one foot.

There was no consanguinity between his parents.

It is interesting to note that only the feet show the keratosis in all his affected relatives, whereas this patient has well-marked lesions of the hands as well.

There is a patchy symmetrical keratosis of the palms and soles, affecting mainly the pressure points, and there is some degree of pes cavus. Hyperidrosis is not a feature. There is not the diffuse involvement of surface that is seen in tylosis, nor are there the fine pitted lesions of punctate keratosis. While the general appearance suggests callosities, the persistence of the condition is against a simple mechanical origin.

The family history as far as it goes points to the trait being inherited as a regular Mendelian dominant. This is in keeping with previous observations on families showing keratoderma disseminatum palmaris et plantaris.

The President: I have seen one case, in a girl, but she was an unco-operative subject. At the time I tried to read up the literature, but it is very difficult to find any classification or grouping, and there seem to be very few cases published.

Lichen Nitidus.—J. R. SIMPSON, M.B. (for H. J. WALLACE, M.D.).

Terence D., aged 9 years.

History.—The eruption was first noticed on the abdomen in March 1946. Since then there has been a steady spread to many other areas, with no evidence of resolution anywhere. There has been no itching. The mother gives no relevant past or family history. In particular there is no history of skin disease or of tuberculosis.

On examination.—The lesions are minute, wholly discrete papules, varying in size from 0·5 mm. to 2 mm. in diameter, but otherwise of uniform character. Their surfaces are glistening. Some are flat and some are dome-shaped, but all are easily palpable. There is no erythema or scaling and the colour is that of normal skin.

They are grouped together in colonies of varying size, distributed profusely on the trunk and limbs, and also on the penis, the forehead and right cheek. They are not related to the pilo-sebaceous follicles. The mucous membranes and the palms and soles are normal. Nothing abnormal was found on general examination.

Investigations.—X-ray of chest: No abnormality seen. Mantoux test: 1 : 10,000 negative; 1 : 1,000 negative. Biopsy from lesions on the right hypochondrium shows histological features characteristic of lichen nitidus.

Comment.—In view of the original conception that the ætiology of this condition was tuberculous he has been treated with calciferol, 100,000 i.u. daily. He has had that for about a month. So far there has been no improvement, in fact fresh lesions have appeared since he has been having it.

Dr. F. F. Hellier: I am interested in what Dr. Simpson has said about the tuberculous ætiology. There is a good deal of evidence that the condition is closely related to lichen planus. In 1937 (Haynes, H., and Hellier, F. (1937) *Ann. Derm. Syph.*, Paris, 8, 192), I published a case in which there was typical lichen nitidus, very like the lesions in this child, and lichen planus. Histologically the lichen planus lesions were the usual ones, whilst the lichen nitidus papules showed the characteristic tuberculoid structure with giant cells. It would be an extraordinary coincidence if the two lesions were not related in some way. On the other hand, it is striking that each of the two lesions should keep its characteristic histology. Personally I feel that the two are closely related.

Dr. H. C. Semon: Other cases of the association have been recorded in the literature and I have recently seen a middle-aged woman with typical lichen nitidus lesions on the inner aspects of both thighs, pruritus vulvæ and labial œdema. It is more than likely that the lichen nitidus lesions were also present on the vulval mucous membrane as in fact they were on the buccal surface of the palate as a "granular stippling"—a characteristic feature of the eruption in this situation. It is significant in this connexion that lichen nitidus lesions are asymptomatic while those of lichen planus are decidedly the reverse.

Dr. P. J. Feeny: I have seen recently a case exactly like this, with, on the forearms, granuloma annulare. Until the biopsy is ready I am calling it lichen scrofulosorum.

Dr. F. Parkes Weber: This kind of lesion (lichen nitidus), does seem clinically to merge into lichen scrofulosorum. In some patients I think there is a little powderiness of the skin over the lesions. I imagine that the two conditions are in some way ætiologically allied.

Dr. J. R. Simpson: There was no evidence of tuberculosis in this case. I should like to say to Dr. Hellier that I do not subscribe to the tuberculosis theory of this condition, but I thought it might be of interest to use calciferol in this case to see whether it threw any further light upon it. With regard to the treatment with gold, Niles [1] has described a case which responded to treatment with gold sodium thiosulphate. Three injections were given and the case cleared up soon afterwards. Dr. Barber's cases [2] which responded were treated with tincture of iodine by mouth.

REFERENCES

1 *Arch. Derm. Syph.*, 1930, **22**, 687.
2 *Brit. J. Derm.*, 1826. 38, 143.

Effect of Calciferol on Lupus Vulgaris (Two Cases), Lupus Pernio and Boeck's Sarcoid.—I. R. MARRE, L.R.C.P., M.R.C.S.

Lupus Vulgaris (CASE I)

A. G., a man aged 67, was admitted to hospital on 6.5.46 for carcinoma of rectum, which proved inoperable.

He also had extensive lupus vulgaris of the lateral parts of his cheeks, zygomatic and temporal areas, involving both ears, the right one being bound down by scar tissue. The areas were curiously symmetrical and had been present for at least twenty years. The diagnosis was confirmed histologically.

He was given calciferol 50,000 units three times daily, and was kept on this dose until two weeks ago. There has been steady improvement and the lupus has been replaced by scar tissue with no evidence of activity. It is interesting that his advanced carcinoma and his marked anæmia did not interfere with the action of calciferol.

[Photographs were shown.]

Lupus Vulgaris (CASE II)

Henry E., aged 46, presented himself in July 1946, with extensive lupus vulgaris involving both cheeks and the adjacent parts of the neck.

The disease had been present for over thirty years, and he had had no treatment other than a twelve months' course of ultraviolet light, and various ointments.

He was given calciferol (50,000 units three times daily) at once, and has been on this dose ever since. He has shown marked improvement, large areas having healed.

Lupus Pernio

Mrs. J. S., aged 43, first attended hospital in September 1944, with a single blue *granulomatous* lesion, affecting the tip and about one-third of the area of her nose. She was treated by Kromayer lamp with "some benefit."

I first saw her in October 1945, when she thought the condition much the same.

The area was just as extensive, and diascopy showed apple-jelly nodules. She was given a short course of myocrisin, and did well, only to relapse shortly afterwards.

In January 1946 she was started on calciferol 50,000 units twice daily, and improvement was apparent, but slow. In April 1946 the dose was increased to 50,000 units three times daily, and the rate of improvement accelerated considerably, until in August 1946 the nose appeared normal. After three weeks' rest, however, the nose appeared much bluer, and treatment was recommenced in September 1946 again with marked improvement.

In October 1945 her chest X-ray was normal and her Mantoux (1 : 1,000) ++.

Boeck's Sarcoid

Mrs. M. A., aged 37. I first showed this woman to the Section in February 1944 (*Proc. R. Soc. Med.*, 37, 411), when the diagnosis of Boeck's sarcoid was agreed and confirmed histologically.

Before and since that time she has had every conceivable treatment with no good effect, and in fact she got steadily worse until May 1945. She still had her original lesions on the left big and second toes and the outer border of the left foot, a patch on the right third toe and outer border of the right foot, a large blue patch on the left cheek, and a swelling on the right side of the nose. This swelling increased enormously in size until in the early part of this year the lower part of the inner canthus on the right side was quite hidden.

On February 7, 1946, calciferol 100,000 units daily was started, and within a month there was a marked decrease in size of the nose.

In April 1946 the dose was increased to 150,000 units and she continued to improve very rapidly. She has continued on this dose with an occasional week's rest until two or three weeks ago, when the calciferol was stopped, and she is now very much better than she has been since 1943.

On the left foot the second toe is much smaller, and the swelling on the outer border has almost disappeared. On the right foot the little toe is smaller and the outer border seems normal. The nose has decreased considerably in size until it is almost normal and she finds herself able to go out without embarrassment.

Dr. J. E. M. Wigley: I should like to ask the exhibitor whether he has had any blood chemistry done in these cases to see whether there is any correlation between alterations in blood chemistry and clinical improvement or between alterations in blood chemistry and symptoms. In my department we have been working on about twenty cases recently, and it has been found that the serum calcium on the whole remains fairly constant, but the variations in the serum calcium do not seem to correspond in any way with the clinical improvement or lack of improvement.

The most important indication we have found has been in the chemistry not of the calcium, but of the allied substance—phosphorus. The fall in the serum alkaline phosphatase is likely to precede the rise in the serum calcium and also to be associated with the onset of symptoms. So far we have not found any serious signs in the way of calcium deposits: some cases have shown deposits, but on stopping the calciferol for a month or two they have disappeared.

The advisability of continuing the maximum dose, or of reducing the dose, or of stopping the calciferol altogether is bound up with the whole subject of the blood chemistry. Then the question arises whether calciferol acts locally or generally. This is a very difficult problem, and we are beginning to tackle it by applying the calciferol in an oily emulsion locally. It appears to be absorbed, and if we can produce the same results on the lesions with locally applied calciferol it will be a great advantage over the general use. We have also tried calciferol in cases where the histological findings were suggestive, rather than on what I may call the vague feeling that they were suitable. One case is of lupus miliaris facei, which has begun to respond to the local application of calciferol, after the general administration had failed. The histology of granuloma annulare is a little suggestive of tuberculosis, but in the one case in which we have tried calciferol, there has been no response to either local or general use of calciferol.

Dr. W. J. O'Donovan: Arising out of Dr. Wigley's remarks he will be interested to hear that I have under my care an elderly woman with severe lupus tumidus of her face of many years' standing and recent granuloma annulare on the back of her right hand. Under treatment with calciferol her lupus has disappeared. The granuloma annulare remains unaffected.

Dr. P. J. Feeny: If Dr. Wigley is able to show that calciferol applied locally will be of the same benefit as calciferol given internally, it will be a great advance in therapy, because serious toxic effects as distinct from symptoms of intolerance following administration internally have already been described in the literature. Apart from dermatological cases, a case of hypoparathyroidism has been published in which the dosage of calciferol used in dermatology caused arterial calcification (Eaton, J. C. (1946) *Biochem. J.*, 40, 52).

Dr. Prosser Thomas: I have tried calciferol locally in several cases of lupus vulgaris without appreciable response.

Sarcoidosis Treated with Calciferol.—BRIAN RUSSELL, M.D.

Mrs. E. B., aged 31.

History.—Two and a half years ago "cyst" on left cheek; was incised but recurred. One year ago similar swelling appeared on right cheek. Ten months ago swellings appeared in skin over both shoulders. Has suffered for many years from psoriasis.

Family history.—Father died of pulmonary tuberculosis twenty three years ago.

On examination (15.5.46).—In both cheeks are symmetrical subcutaneous, partly intradermal nodules of bluish colour with overlying telangiectatic erythema. Koilonychia. Psoriasis of elbows of long duration. Similar subcutaneous nodules about 1 cm. in diameter over upper deltoid region of both shoulders. No enlargement of lymphatic glands. Liver and spleen not palpable.

Investigations.—Biopsy from one of the arm lesions shows a granuloma of the dermis with a few giant cells and much round-cell infiltration but no caseation. Ziehl-Neelsen sections and Gram and modified Ziehl-Neelsen 5% sections show no organisms. Blood Wassermann and Kahn reactions negative. Graduated Mantoux test—weakly positive 1 : 1,000.

X-ray of hands—no abnormality detected, chest—marked hilar glandular enlargements.

Blood-count.—R.B.C. 5,730,000 per c.mm., Hb. 90%, C.I. 0·78%. W.B.C. 9,300 per c.mm. Differential: Polys. 84%, eosinos. and lymphos. 16%.

Sedimentation rates.—25.6.46: 25 mm. corrected; 24.7.46: 32 mm. corrected; 4.9.46: 24 mm. corrected.

Treatment.—The patient has received 50,000 units of calciferol twice a day since 9.6.46 and extra milk.

9.10.46: The lesions on the face are now softer and flatter. On the shoulders there remains only a discoloration. Involutionary changes therefore appear to be taking place in the cutaneous lesions but not in the glandular lesions, as two further X-ray films (7.8.46 and 2.10.46) reveal no alteration in the size of the hilar opacities. The erythrocyte sedimentation rate shows no improvement.

Case for Diagnosis. ? Reticulosis. ? Circumscribed Myxœdema.—BRIAN RUSSELL, M.D.

Mrs. L. V., aged 48.

History.—1943: Operation for adenomatous goitre. November 1944: pneumonia and ? pulmonary abscess, treated with sulphapyridine and penicillin. December 1945: noticed discoloration and thickening of the skin between brows and on cheeks and forearms. The condition is aggravated by hot tea or coffee, and by excitement and exertion. Catamenia have ceased. She has never been abroad but has had much exposure to sunlight in youth, having been a Land Girl on her father's farm 1914-18, a keen gardener and "outdoor person". She was very freckled in youth.

On examination (21.5.46).—Alert woman, of normal build. Waxy-looking, symmetrical, sharply marginated, infiltrated, intradermal red plaques of cartilaginous consistency between brows, over forehead in three finger-like processes, on malar regions and alæ nasi with associated telangiectasia. Eyebrows are thin. Tonsils are not enlarged. Has dentures. Scar of thyroid operation on neck. On sides of neck there is a patchy, reticular, brownish-red pigmentation with atrophic changes but without infiltration. On outer arms and extensor surface of forearms and proximal phalanges of fingers there is a confluent, papular, infiltrated, non-pruritic erythema, with numerous small, outlying, whitish nodules at shoulders. No areas of anæsthesia detected. No enlargement of lymphatic glands. Liver and spleen not palpable. Groups of firm, pinkish nodules just above both knees, and over inner calves.

Investigations.—Blood Wassermann and Kahn reactions negative. Graduated Mantoux test—weakly positive 1 : 10.000.

Blood-count.—Hb. 95%. W.B.C. 7,600 per c.mm. Differential: Polys. 57%, lymphos. 36%, monos. 5%, eosinos. 1%, basos. 1%.

Biopsy from infiltrated facial lesion shows thinned epidermis and very numerous, closely packed, pale endothelioid cells between the collagen bundles, involving almost the whole of the corium. Histology of arm lesions similar. No acid-fast bacilli in either.

X-ray of hands—no abnormality detected; chest—slightly increased hilar shadows, particularly right.

Treatment.—A dose of 400 r X-rays has been applied to the upper half of the lesion on the left forearm, but without effect other than slight increase in pigmentation.

Thyroid extract has been administered for the last two weeks before this meeting.

19.11.46: The patient complains of palpitations and throbbing in the throat since taking the thyroid tablets. This treatment has therefore been stopped. The dose was at first ½ grain twice a day but for the past two weeks has been 1 grain twice a day.

It is hoped that this case will be shown again at a future meeting, when Dr. Freudenthal will demonstrate some results of his histological investigations.

Dr. W. Freudenthal: May I suggest that this case belongs to the myxœdema group? In certain aspects, e.g. the aggregated dome-shaped papules, it has some clinical resemblance to P. B. Mumford and H. W. Barber's case of "myxœdema moniliforme" shown at the Royal Society of Medicine on 21.1.43 (*Proc. R. Soc. Med.*, 1943, 36, 286).

Miliary Lymphocytoma.—F. R. BETTLEY, M.R.C.P.

A. G., aged 48.

History.—At age 28 to 31, rash on backs of hands and forearms after exposure to sun and wind. In June, after exposure to the sun at the seaside, burning and weeping rash affecting the face. Similar attack in summer 1939, followed by itching spots which have appeared from time to time on the limbs and trunk ever since. The face still becomes red and sore after exposure to the sun. General health and family history, normal.

Present state.—On admission to hospital: Over the whole of the forehead, and to a less extent the zygomatic, malar and upper nasal regions the skin contains numerous closely set pinhead-sized semitranslucent grains. They are little raised above the surface of the surrounding skin. Over the trunk and limbs are scattered excoriations No enlargement detected of lymph glands, liver or spleen. General medical examination normal. X-ray of chest normal. W.R. negative. Blood urea normal, but Van Slyke renal function test 44% of normal.

Blood-count.—Hb. 93%. W.B.C. 5,800, neutros. 55%, lymphos. 40%, monos. 3%, eosinos. 1%.

Biopsy from forehead (Prof. R. W. Scarff): There is partial separation of the stratum corneum, but the epithelium is otherwise normal. In the middle of the dermis are circumscribed areas of lymphoid tissue. The smaller areas are made up of lymphocytes: the larger areas contain in addition lymphoblasts and large reticulo-endothelial cells, with well-marked follicular structure. In some of the sections there is a suggestion that some of these are related to sweat glands, but this relationship cannot be established in most instances.

Mercury-vapour lamp.—One-half and five-sixths of the normal first degree erythema dose was given to areas on the back of the thorax. After six hours both areas tested showed marked redness with œdema.

Dr. A. C. Roxburgh: I happen to have two patients—sisters—both of whom show this sort of condition. In both cases the lesions are on the temples and in one they are also on the left malar region. The lesions look like cysts but they are, I feel sure, the same as in this case.

Dr. Bettley: I believe that for the most part in the cases previously described this condition is stated to give rise to something larger in the way of tumours, up to the size of a pea, more grouped and localized and very often of a dark red colour. My recollection is that Epstein (S. Epstein, 1935, *Arch. Derm. Syph.*, 173, 181), who recorded, I think, four cases of this kind, mentioned one which has practically all the features of the case now shown—the light sensitivity, the itchy eruption over most of the body, and the quite small miliary lesions, rather suggesting, as Dr. Roxburgh says, cysts.

Dermatitis Bullosa Striata Pratensis.—H. GRUEBEL LEE, M.B., Ch.B. (introduced by Dr. I. MUENDE).

The patient, a woman aged 33, was first seen in the out-patients' department of Redhill County Hospital on October 7, 1946, complaining of irregularly shaped pigmented lesions on the forearms and legs, of five weeks' duration. The eruption strongly resembled that first described by Oppenheim in 1926 as Ottakring dermatitis, later as Bad und Wiesen dermatitis, and eventually as dermatitis bullosa striata pratensis; and the history confirmed this diagnosis.

The patient stated that the first signs of the affection were noticed shortly after weeding among parsnip beds at Hersham, near Walton-on-Thames. She spent four hours the first day and two the following morning, wearing a short-sleeved blouse, shorts and woollen stockings, but later removed the stockings on account of the heat. She was exposed to bright sunshine, and about forty-eight hours later she noticed wheals, with central tense bullæ, developing on the anterior surfaces of the legs and the anterior and inner aspects of the forearms. These were associated with severe irritation, which was relieved by pricking the blisters with a needle.

She had no further trouble, the affection resolving without any internal treatment or local application, and leaving brownish pigmentation. There is no previous history of dermatitis or of light sensitivity.

O'Donovan [1] reviewed two minor epidemics of dermatitis due to plant contact in the hot season, and pointed out that all the clinical characteristics of acuteness, the production of linear markings and blisters, and the artificial bizarre appearance of the eruption had developed in these cases as in previous records. The weed, *Agrimonia eupatoria*, was held as the cause of the epidemics, although O'Donovan was of the opinion that it is not the only cause of dermatitis bullosa striata pratensis in England. The late Dr. Robert Klaber [2] made a valuable contribution to the subject, and suggested that, in view of the fact that the eruption appeared to be due to light sensitivity following contact with certain plants, the title *phyto-photo-dermatitis* be employed in these cases.

I conducted patch tests on October 14 with leaf and stem of the same species of parsnip. The result, read after forty-eight hours, was positive with the leaf, and slightly more so in the case of the stem. I feel, however, that the test should have been followed by exposure of the part to the sun, or to the action of ultraviolet light; but unfortunately time did not permit.

REFERENCES

1 O'DONOVAN, W. J. (1942) *Brit. J. Derm.*. 54, 39.
2 KLABER, R. (1942) *Brit. J. Derm.*, 54, 193.

Dr. F. F. Hellier: In a group of cases of this condition on Salisbury Plain at the beginning of the war, it was at first thought that the men had been attacked by mustard gas, but a dermatologist diagnosed the true condition. I had a similar experience in Belgium where two girls had been handling parsnips, and it was thought that someone had put mustard gas on the parsnips. The true explanation was very simple. It was fine weather and the girls thought that it would be nice to peel the parsnips out of doors instead of indoors, with the result that they got a bullous dermatitis of the hands due to exposing the skin to sunlight after it had been sensitized by the juice of the parsnips.

Dr. C. H. Whittle: I recall two girls, whose occupation was canning parsnips, who showed a strikingly pellagrous type of eruption on the back of the hands. I saw these cases in the middle of the war and was unable to do anything about a follow-up or investigation, e.g. vitamin B estimation and therapy. The eruption followed exposure to the sun—it was in July—and came on while they were canning the parsnips. There have been reports in the literature of cases among canners who have shown the same type of eruption, e.g. Starck, Vera, 1944, *Acta. Dermat.-venereal.*, 25, 179 (quoted by Sulzberger, 1945 Year Book of Dermatology). In the 13 cases described the lesions followed exposure to the sun and involved the back of the hands, and forearms if exposed. 6 other women similarly exposed did not develop dermatitis. It is possible that the 13 reacting cases were deficient in vitamin B.

Section of Physical Medicine

President—FRANK COOKSEY, O.B.E., M.D.

[*November* 13, 1946]

Physiotherapy in an Accident Service

By Sir MAX PAGE, K.B.E., C.B., M.S.

THE importance of the application of physical methods in rehabilitation after injury is generally recognized, and calls for close collaboration between surgeon and physiotherapist.

The reaction of the surgeon to physiotherapy has varied widely through the ages. The classical writers recognized and sometimes described in detail the use of massage and exercises, but in general they directed the use of these procedures to the maintenance of health or the cure of disease rather than to rehabilitation after injury. It is, however, true that in the Hippocratic canon careful instructions are found on the use of massage and early movement after dislocation of the shoulder.

That great universalist, Galen, records his experiences when, early in his career, he was medical officer in charge of the gladiatorial school at Pergamum. I have not read his original account, but from abstracts it would appear that his main pride was in the fact that during his service he never lost the life of a wounded man; this he attributes to his method of wound dressing—which indeed was of a mildly antiseptic character. In his later writings on medical gymnastics his views are noticeably modern: he divided exercises into the passive type, including therein massage, and active exercises such as ball games and walking, and mixed, which he exemplified by horse riding.

His suggestive work was in some degree incorporated into the Arabian school of medicine but does not seem to have found any place in the practice of later European surgeons. It is indeed surprising how little reference to the restoration of function after injury is found in the writings of the latter. It remains a matter of opinion whether this was due to the greater toughness of frame and spirit of our forebears or whether to a more placid acceptance of disability after injury than is common nowadays. It should not be overlooked that the exploitation and advertisement of physiotherapeutic procedures by quacks led to a prejudice against their practice among the regular members of the profession. In any case the circumstances may and localized and very often of a dark red colour. My recollection is that Epstein (S. Epstein, 1935, *Arch. Derm. Syph.*, 173, 181), who recorded, I think, four cases of this kind, mentioned one which has practically all the features of the case now shown—the light sensitivity, the itchy eruption over most of the body, and the quite small-miliary lesions, rather suggesting, as Dr. Roxburgh says, cysts.

Dermatitis Bullosa Striata Pratensis.—H. GRUEBEL LEE, M.B., Ch.B. (introduced by Dr. I. MUENDE).

The patient, a woman aged 33, was first seen in the out-patients' department of Redhill County Hospital on October 7, 1946, complaining of irregularly shaped pigmented lesions on the forearms and legs, of five weeks' duration. The eruption strongly resembled that first described by Oppenheim in 1926 as Ottakring dermatitis, later as Bad und Wiesen dermatitis, and eventually as dermatitis bullosa striata pratensis; and the history confirmed this diagnosis.

The patient stated that the first signs of the affection were noticed shortly after weeding among parsnip beds at Hersham, near Walton-on-Thames. She spent four hours the first day and two the following morning, wearing a short-sleeved blouse, shorts and woollen stockings, but later removed the stockings on account of the heat. She was exposed to bright sunshine, and about forty-eight hours later she noticed wheals, with central tense bullæ, developing on the anterior surfaces of the legs and the anterior and inner aspects of the forearms. These were associated with severe irritation, which was relieved by pricking the blisters with a needle.

She had no further trouble, the affection resolving without any internal treatment or local application, and leaving brownish pigmentation. There is no previous history of dermatitis or of light sensitivity.

O'Donovan [1] reviewed two minor epidemics of dermatitis due to plant contact in the hot season, and pointed out that all the clinical characteristics of acuteness, the production of linear markings and blisters, and the artificial bizarre appearance of the eruption had developed in these cases as in previous records. The weed, *Agrimonia eupatoria*, was held as the cause of the epidemics, although O'Donovan was of the opinion that it is not the only cause of dermatitis bullosa striata pratensis in England. The late Dr. Robert Klaber [2] made a valuable contribution to the subject, and suggested that, in view of the fact that the eruption appeared to be due to light sensitivity following contact with certain plants, the title *phyto-photo-dermatitis* be employed in these cases.

I conducted patch tests on October 14 with leaf and stem of the same species of parsnip. The result, read after forty-eight hours, was positive with the leaf, and slightly more so in the case of the stem. I feel, however, that the test should have been followed by exposure of the part to the sun, or to the action of ultraviolet light; but unfortunately time did not permit.

REFERENCES

1 O'DONOVAN, W. J. (1942) *Brit. J. Derm.*, 54, 39.
2 KLABER, R. (1942) *Brit. J. Derm.*, 54, 193.

Dr. F. F. Hellier: In a group of cases of this condition on Salisbury Plain at the beginning of the war, it was at first thought that the men had been attacked by mustard gas, but a dermatologist diagnosed the true condition. I had a similar experience in Belgium where two girls had been handling parsnips, and it was thought that someone had put mustard gas on the parsnips. The true explanation was very simple. It was fine weather and the girls thought that it would be nice to peel the parsnips out of doors instead of indoors, with the result that they got a bullous dermatitis of the hands due to exposing the skin to sunlight after it had been sensitized by the juice of the parsnips.

Dr. C. H. Whittle: I recall two girls, whose occupation was canning parsnips, who showed a strikingly pellagrous type of eruption on the back of the hands. I saw these cases in the middle of the war and was unable to do anything about a follow-up or investigation, e.g. vitamin B estimation and therapy. The eruption followed exposure to the sun—it was in July—and came on while they were canning the parsnips. There have been reports in the literature of cases among canners who have shown the same type of eruption, e.g. Starck, Vera, 1944, *Acta. Dermat.-venereal.*, 25, 179 (quoted by Sulzberger, 1945 Year Book of Dermatology). In the 13 cases described the lesions followed exposure to the sun and involved the back of the hands, and forearms if exposed. 6 other women similarly exposed did not develop dermatitis. It is possible that the 13 reacting cases were deficient in vitamin B.

in the special fracture and accident clinics now common, the average standard of results shows a considerable advance on those of twenty years ago. The part played by surgeon and physiotherapist in these organizations is by no means rigidly fixed and is subject to considerable variation, but I will put forward a scheme which I think can be a successful one, fully admitting that wide diversity in method is necessary in order to suit different types of hospital and the varying personalities involved.

We have observed that in the past both the physiotherapist as well as the surgeon can be successful organizers of fracture departments. Not unnaturally I favour control by a surgeon and the organization I roughly sketch is founded mainly on experience in a large teaching hospital. The working medical personnel of the team should consist of a surgical director and one or two senior assistants together with corresponding house officers, two plaster Sisters and two or three certificated physiotherapists. The numbers in each category will clearly depend on the size of the clinic. The physiotherapists should take their instructions direct from the surgeon in charge; they should be handpicked for the job. From their training a reasonable knowledge of the standard methods of treatment may be assumed. but it is of great importance that they should possess firm personalities and have the ability to inspire their patients to work—in the sense of carrying out active movement. These ladies should be closely incorporated in the team, attending both ward rounds and outpatient clinics. The medical officer in charge of the department of physical medicine will only come into the picture as a consultant, the manner of which I will refer to later.

Physiotherapy departments tend to become overloaded with a mass of human material. Unless regular and rigorous checks are imposed a certain number of patients continue under treatment for months with little benefit to themselves and to the prejudice of the more deserving. It is in the main department, so often the dumping ground filled by various overworked clinicians, that this state of affairs is most in evidence: but similar crowding may affect the accident service if certain precautions are not taken. Overloading can be avoided or reduced if the needs of each individual case for physiotherapy are carefully estimated. First, most children, the subject of fracture, require little or no physiotherapeutic help in order to make a complete and speedy recovery. Adults should be classified into four groups in accordance with which the time they spend with the therapist may be determined. My idea of these groups is as follows:

(1) The enterprising—possessed of a love of personal independence and an attitude of self-help.
(2) The average co-operator.
(3) The poor-spirited and self-centred type.
(4) The non-co-operator derived from group 3 or such reasons as interest in compensation or a love of sympathy.

The physiotherapist in handling group 1 has only to make clear to the patient what freedom is permissible and demonstrate the appropriate exercises.

Group 2 will require more help and supervision and sometimes a certain amount of auxiliary treatment of the nature of massage or faradism.

It is those in the remaining two groups that strain our patience and judgment to the utmost. They should be brought before the medical officer i/c of Physical Medicine at a weekly consultation. At this consultation his opinion as to suitable treatment for difficult cases or those hanging fire is obtained and the psychological

remind us that a good recovery after injury is effected often enough without the intervention of any specialized treatment.

Even in the eighteenth century among surgical writers it is only John Hunter who approaches the problems of injury scientifically. His study of the physiology of muscular action and its application to the treatment of stiff joints remains a landmark. Surgeons as a whole, however, in the treatment of fractures continued to concentrate on methods of fixation: movement was left to return as it might after firm union was present. Adherents of the Ling school of gymnastics, established in 1816, and of the Zander system of mechanotherapy (1864) certainly used their special procedures in some cases of disability after injury, but these methods were not incorporated into the normal practice of current surgery.

It was undoubtedly Lucas-Championnière who first attacked the ruling faith in the value of rigid and prolonged fixation for all fractures, and I think his work in this respect deserves fuller recognition than it has so far received. One may recall that he was a general surgeon practising in Paris and one who had early in his career provoked the enmity of some of his colleagues on account of his prompt and ardent support of Lister. He published "Le Mouvement est la Vie" in 1880 and in 1886 first announced his method of treating fractures by mobilization and massage. It is evident that his suggestions met with a chilly reception for in his later book entitled "Le Mobilisation et le Massage dans le Traitement de Fractures" he says "Le public est peu preparé à accepter ce traitement revolutionnaire. Le monde médical n'y est pas beaucoup plus preparé que le public." He approached the problem with caution and selective judgment. At first he applied the method only to fractures of the lower end of the radius and of the fibula; subsequently to the upper extremity of the humerus. He recognized its limitations in the management of the major fractures of the long bones of the lower limb and he was always an advocate of the operative suture of the broken patella or olecranon. He laid great importance on massage of the limb soon after injury and instructed his students and assistants in a simple technique, being somewhat critical of the existing school of massage.

I think one of the reasons for the poor support given to Lucas-Championnière was the counterattraction exercised by the methods of open fixation of fractures which were introduced about the same time by Lane and Lambotte. This new technique undoubtedly made a strong appeal to the enterprising young surgeon—a nice piece of carpentry and a good-looking radiograph seemed to terminate his responsibility. In this country it was not till 1912 that a successful out-patient clinic based on Lucas-Championnière's teaching was organized by Dr. J. B. Mennell at St. Thomas's Hospital.

In the first great war the demand for systematic rehabilitation after injury was met by the organizations inspired by Sir Robert Jones and his school. The application of most of the conceivable forms of physical energy were then or later tried out. By a gradual process of trial and failure those found useful have been incorporated into the body of physiotherapeutic practice to-day.

In this period a break in the traditional methods of fracture management should be remembered, viz. that of Bohler of Vienna. In his clinic he obtained good results and shortened the average period of disability by postural treatment coupled with systematic active exercise; all forms of physiotherapy being dispensed with. I think his teaching has exerted a considerable influence on the practice of fracture clinics in this country.

With this wealth of experience behind us we may ask what position in this relationship we have arrived at to-day. There is, I think, general agreement that.

in the special fracture and accident clinics now common, the average standard of results shows a considerable advance on those of twenty years ago. The part played by surgeon and physiotherapist in these organizations is by no means rigidly fixed and is subject to considerable variation, but I will put forward a scheme which I think can be a successful one, fully admitting that wide diversity in method is necessary in order to suit different types of hospital and the varying personalities involved.

We have observed that in the past both the physiotherapist as well as the surgeon can be successful organizers of fracture departments. Not unnaturally I favour control by a surgeon and the organization I roughly sketch is founded mainly on experience in a large teaching hospital. The working medical personnel of the team should consist of a surgical director and one or two senior assistants together with corresponding house officers, two plaster Sisters and two or three certificated physiotherapists. The numbers in each category will clearly depend on the size of the clinic. The physiotherapists should take their instructions direct from the surgeon in charge; they should be handpicked for the job. From their training a reasonable knowledge of the standard methods of treatment may be assumed but it is of great importance that they should possess firm personalities and have the ability to inspire their patients to work—in the sense of carrying out active movement. These ladies should be closely incorporated in the team, attending both ward rounds and outpatient clinics. The medical officer in charge of the department of physical medicine will only come into the picture as a consultant, the manner of which I will refer to later.

Physiotherapy departments tend to become overloaded with a mass of human material. Unless regular and rigorous checks are imposed a certain number of patients continue under treatment for months with little benefit to themselves and to the prejudice of the more deserving. It is in the main department, so often the dumping ground filled by various overworked clinicians, that this state of affairs is most in evidence: but similar crowding may affect the accident service if certain precautions are not taken. Overloading can be avoided or reduced if the needs of each individual case for physiotherapy are carefully estimated. First, most children, the subject of fracture, require little or no physiotherapeutic help in order to make a complete and speedy recovery. Adults should be classified into four groups in accordance with which the time they spend with the therapist may be determined. My idea of these groups is as follows:

(1) The enterprising—possessed of a love of personal independence and an attitude of self-help.
(2) The average co-operator.
(3) The poor-spirited and self-centred type.
(4) The non-co-operator derived from group 3 or such reasons as interest in compensation or a love of sympathy.

The physiotherapist in handling group 1 has only to make clear to the patient what freedom is permissible and demonstrate the appropriate exercises.

Group 2 will require more help and supervision and sometimes a certain amount of auxiliary treatment of the nature of massage or faradism.

It is those in the remaining two groups that strain our patience and judgment to the utmost. They should be brought before the medical officer i/c of Physical Medicine at a weekly consultation. At this consultation his opinion as to suitable treatment for difficult cases or those hanging fire is obtained and the psychological

remind us that a good recovery after injury is effected often enough without the intervention of any specialized treatment.

Even in the eighteenth century among surgical writers it is only John Hunter who approaches the problems of injury scientifically. His study of the physiology of muscular action and its application to the treatment of stiff joints remains a landmark. Surgeons as a whole, however, in the treatment of fractures continued to concentrate on methods of fixation: movement was left to return as it might after firm union was present. Adherents of the Ling school of gymnastics, established in 1816, and of the Zander system of mechanotherapy (1864) certainly used their special procedures in some cases of disability after injury, but these methods were not incorporated into the normal practice of current surgery.

It was undoubtedly Lucas-Championnière who first attacked the ruling faith in the value of rigid and prolonged fixation for all fractures, and I think his work in this respect deserves fuller recognition than it has so far received. One may recall that he was a general surgeon practising in Paris and one who had early in his career provoked the enmity of some of his colleagues on account of his prompt and ardent support of Lister. He published "Le Mouvement est la Vie" in 1880 and in 1886 first announced his method of treating fractures by mobilization and massage. It is evident that his suggestions met with a chilly reception for in his later book entitled "Le Mobilisation et le Massage dans le Traitement de Fractures" he says "Le public est peu preparé à accepter ce traitement revolutionnaire. Le monde médical n'y est pas beaucoup plus preparé que le public." He approached the problem with caution and selective judgment. At first he applied the method only to fractures of the lower end of the radius and of the fibula; subsequently to the upper extremity of the humerus. He recognized its limitations in the management of the major fractures of the long bones of the lower limb and he was always an advocate of the operative suture of the broken patella or olecranon. He laid great importance on massage of the limb soon after injury and instructed his students and assistants in a simple technique, being somewhat critical of the existing school of massage.

I think one of the reasons for the poor support given to Lucas-Championnière was the counterattraction exercised by the methods of open fixation of fractures which were introduced about the same time by Lane and Lambotte. This new technique undoubtedly made a strong appeal to the enterprising young surgeon—a nice piece of carpentry and a good-looking radiograph seemed to terminate his responsibility. In this country it was not till 1912 that a successful out-patient clinic based on Lucas-Championnière's teaching was organized by Dr. J. B. Mennell at St. Thomas's Hospital.

In the first great war the demand for systematic rehabilitation after injury was met by the organizations inspired by Sir Robert Jones and his school. The application of most of the conceivable forms of physical energy were then or later tried out. By a gradual process of trial and failure those found useful have been incorporated into the body of physiotherapeutic practice to-day.

In this period a break in the traditional methods of fracture management should be remembered, viz. that of Bohler of Vienna. In his clinic he obtained good results and shortened the average period of disability by postural treatment coupled with systematic active exercise; all forms of physiotherapy being dispensed with. I think his teaching has exerted a considerable influence on the practice of fracture clinics in this country.

With this wealth of experience behind us we may ask what position in this relationship we have arrived at to-day. There is, I think, general agreement that.

in the special fracture and accident clinics now common, the average standard of results shows a considerable advance on those of twenty years ago. The part played by surgeon and physiotherapist in these organizations is by no means rigidly fixed and is subject to considerable variation, but I will put forward a scheme which I think can be a successful one, fully admitting that wide diversity in method is necessary in order to suit different types of hospital and the varying personalities involved.

We have observed that in the past both the physiotherapist as well as the surgeon can be successful organizers of fracture departments. Not unnaturally I favour control by a surgeon and the organization I roughly sketch is founded mainly on experience in a large teaching hospital. The working medical personnel of the team should consist of a surgical director and one or two senior assistants together with corresponding house officers, two plaster Sisters and two or three certificated physiotherapists. The numbers in each category will clearly depend on the size of the clinic. The physiotherapists should take their instructions direct from the surgeon in charge; they should be handpicked for the job. From their training a reasonable knowledge of the standard methods of treatment may be assumed but it is of great importance that they should possess firm personalities and have the ability to inspire their patients to work—in the sense of carrying out active movement. These ladies should be closely incorporated in the team, attending both ward rounds and outpatient clinics. The medical officer in charge of the department of physical medicine will only come into the picture as a consultant, the manner of which I will refer to later.

Physiotherapy departments tend to become overloaded with a mass of human material. Unless regular and rigorous checks are imposed a certain number of patients continue under treatment for months with little benefit to themselves and to the prejudice of the more deserving. It is in the main department, so often the dumping ground filled by various overworked clinicians, that this state of affairs is most in evidence: but similar crowding may affect the accident service if certain precautions are not taken. Overloading can be avoided or reduced if the needs of each individual case for physiotherapy are carefully estimated. First, most children, the subject of fracture, require little or no physiotherapeutic help in order to make a complete and speedy recovery. Adults should be classified into four groups in accordance with which the time they spend with the therapist may be determined. My idea of these groups is as follows:

(1) The enterprising—possessed of a love of personal independence and an attitude of self-help.
(2) The average co-operator.
(3) The poor-spirited and self-centred type.
(4) The non-co-operator derived from group 3 or such reasons as interest in compensation or a love of sympathy.

The physiotherapist in handling group 1 has only to make clear to the patient what freedom is permissible and demonstrate the appropriate exercises.

Group 2 will require more help and supervision and sometimes a certain amount of auxiliary treatment of the nature of massage or faradism.

It is those in the remaining two groups that strain our patience and judgment to the utmost. They should be brought before the medical officer i/c of Physical Medicine at a weekly consultation. At this consultation his opinion as to suitable treatment for difficult cases or those hanging fire is obtained and the psychological

outlook of the individual is discussed. It may also be that he is specially interested in some of the snags of an accident service, such as suspected ruptures of the supraspinatus tendon, the condition known as frozen shoulder, or even low back pain.

The ideas I have roughed out apply to what appear to be straighforward cases and I will not confuse the issue by discussing the management of nerve injuries or other complications.

A word on Rehabilitation Centres. During the war these have fully proved their value in the management of bulk casualties. I am not sure of the degree to which they can be usefully employed in normal civil life. I think that in a well-established accident clinic most cases of injury can be seen through to full recovery by the team primarily responsible for their treatment. "Passing the buck", however, is always popular and sometimes it benefits the patient. Certainly the final tuning up after major injuries is best conducted in fair-sized classes, but God forfend the time when everyone who sustains a fracture thinks he cannot return to work till he has passed through a rehabilitation centre.

Dr. John H. Crosland: I would like to outline a few methods as to how we, as physical medicine specialists, can assist the orthopædic surgeon to attain the common aim of the fullest possible restoration of function to the patient.

A large number of orthopædic patients are perfectly healthy individuals leading a normal active life until they are knocked down by a bus, or sustain some similar damage. Many of these may be kept in bed for months and, during this time, unless they are helped, they more or less rapidly deteriorate both physically and mentally. It is obvious that such deterioration will also retard recovery of the actually traumatized part. In order to prevent this, the patient should be visited daily by a competent physiotherapist, and every part of his body except that immobilized by the surgeon, or that which when moved will interfere with such immobilization, should be given a full range of active movement. Breathing exercises and active contractions of abdominal and back muscles are all very important and can be given very adequately in the prone position.

Perhaps the cases requiring the most constant and patient treatment of this type are those condemned for a year or more to a plaster bed. Yet all that work is well rewarded when it is time for the patient to get up and it is seen how quickly he walks normally and how relatively good his general muscle tone can be.

I will pass rapidly over such small but important points as leaving a window over the knee-joint in a full-length leg plaster so that the patella can be passively moved twice daily; or, as advocated by some, of leaving another window in such a plaster over the quadriceps so that faradic stimulation may be given, or of leaving adequate room in a plaster so that full toe movements can be given, and come to one of the biggest bugbears. I refer to the stiff knee-joint following prolonged extension of a fractured shaft of femur in a Thomas's splint.

Generally speaking, the earlier a joint can be moved, the less likely is it to become stiff and so I propose to outline a method used to move knee-joints adopted by the orthopædic surgeon at Ashbridge E.M.S. Hospital. The idea is that the leg below the knee shall rest on the hinged extension portion of the Thomas's splint, and skin traction be applied in the normal way with the cord bearing the weight passing over a pulley at the end of the bed. The splint itself must be wide enough for the patient's foot and the hinged portion to pass inside it; it is fixed in abduction and elevated in the usual manner.

Normally, the hinged portion is tied to the main portion of the splint by a piece of string so that the foot projects through the main portion and both portions are in the same plane.

The knee-joint can now be flexed to about 45–50 degrees by simply untying the piece of string and allowing the hinged portion to move slowly and evenly downwards and the traction weights need not be removed or the leg moved in any other way. It is possible to get further flexion by using a bed with a "cut-away" side. This method proved satisfactory in operation and the proper alignment of the fractured femur was not interfered with.

Section of Orthopædics

President—V. H. Ellis, F.R.C.S.

[*October* 1, 1946]

Injuries of the Cervical Vertebræ

PRESIDENT'S ADDRESS

By V. H. Ellis, F.R.C.S.

It is a little more than six years since this subject was most ably discussed before this Society by Eastwood and Jefferson (*Proc. R. Soc. Med.*, 33, 651), but there is still much to be learnt about these injuries, and my experience of the last four years has at any rate taught me a great deal both of the details of management and the progress of the injuries.

There have been references to these injuries in medical literature from 2500 B.C. increasing to a vast quantity in recent years, and I do not propose to review them.

Serious injuries of the cervical spine must always carry a fair mortality, but the decrease in fatal bilateral dislocation from 92·6% in 1869 (Blasius) and 30% in 1930 (Langsworthy) to about 16% in my cases, suggests, unless the series are incomparable, that treatment is still improving, as it is unlikely the injuries are decreasing in severity.

The commonest causes are stated to be motor-car accidents, diving into shallow water and falling downstairs, and my cases confirm this. I have no experience of wounds or compound fractures in this region.

These injuries are usually divided into fractures, fracture-dislocations and dislocations, but with the exception of special types such as fracture of the odontoid, the neural arch or spine, this classification is not of great assistance.

I have had one example of fracture of the arch of the atlas. The mechanism by which this was produced is not clear, but it was apparently a combination of compression and extension, so that the occiput was forced downwards and backwards upon the axis. There was a minor degree of displacement and no evidence of damage to the central nervous system. The patient had severe and persistent pain in the area supplied by the small occipital nerve. The pain was immediately relieved by injecting novocain at the point where the nerve crosses the arch of the atlas, but it tended to recur.

Fractures of the odontoid process are not very uncommon. Those which are displaced are often, but not always, fatal. Fractures without displacement are difficult to diagnose because the bony fusion between the peg and body of the axis is not always complete and so simulates a fracture of the base of the process.

I recall two interesting fractures of the odontoid process with displacement. The first was demonstrated at Lambeth Hospital some years ago.

An old man was admitted to the hospital with retention of urine. When his prostate was examined it was found to be of normal size and on closer inquiry into the history the surgeon found that retention had occurred only on those occasions when the patient had fallen asleep in his chair in front of the fire. He had extensor plantar responses.

There was a history of a fall with acute flexion of the head some time previously, and an X-ray showed gross displacement of the atlas and odontoid process.

outlook of the individual is discussed. It may also be that he is specially interested in some of the snags of an accident service, such as suspected ruptures of the supraspinatus tendon, the condition known as frozen shoulder, or even low back pain.

The ideas I have roughed out apply to what appear to be straighforward cases and I will not confuse the issue by discussing the management of nerve injuries or other complications.

A word on Rehabilitation Centres. During the war these have fully proved their value in the management of bulk casualties. I am not sure of the degree to which they can be usefully employed in normal civil life. I think that in a well-established accident clinic most cases of injury can be seen through to full recovery by the team primarily responsible for their treatment. "Passing the buck", however, is always popular and sometimes it benefits the patient. Certainly the final tuning up after major injuries is best conducted in fair-sized classes, but God forfend the time when everyone who sustains a fracture thinks he cannot return to work till he has passed through a rehabilitation centre.

Dr. John H. Crosland : I would like to outline a few methods as to how we, as physical medicine specialists, can assist the orthopædic surgeon to attain the common aim of the fullest possible restoration of function to the patient.

A large number of orthopædic patients are perfectly healthy individuals leading a normal active life until they are knocked down by a bus, or sustain some similar damage. Many of these may be kept in bed for months and, during this time, unless they are helped, they more or less rapidly deteriorate both physically and mentally. It is obvious that such deterioration will also retard recovery of the actually traumatized part. In order to prevent this, the patient should be visited daily by a competent physiotherapist, and every part of his body except that immobilized by the surgeon, or that which when moved will interfere with such immobilization, should be given a full range of active movement. Breathing exercises and active contractions of abdominal and back muscles are all very important and can be given very adequately in the prone position.

Perhaps the cases requiring the most constant and patient treatment of this type are those condemned for a year or more to a plaster bed. Yet all that work is well rewarded when it is time for the patient to get up and it is seen how quickly he walks normally and how relatively good his general muscle tone can be.

I will pass rapidly over such small but important points as leaving a window over the knee-joint in a full-length leg plaster so that the patella can be passively moved twice daily; or, as advocated by some, of leaving another window in such a plaster over the quadriceps so that faradic stimulation may be given, or of leaving adequate room in a plaster so that full toe movements can be given, and come to one of the biggest bugbears. I refer to the stiff knee-joint following prolonged extension of a fractured shaft of femur in a Thomas's splint.

Generally speaking, the earlier a joint can be moved, the less likely is it to become stiff and so I propose to outline a method used to move knee-joints adopted by the orthopædic surgeon at Ashbridge E.M.S. Hospital. The idea is that the leg below the knee shall rest on the hinged extension portion of the Thomas's splint, and skin traction be applied in the normal way with the cord bearing the weight passing over a pulley at the end of the bed. The splint itself must be wide enough for the patient's foot and the hinged portion to pass inside it ; it is fixed in abduction and elevated in the usual manner.

Normally, the hinged portion is tied to the main portion of the splint by a piece of string so that the foot projects through the main portion and both portions are in the same plane.

The knee-joint can now be flexed to about 45–50 degrees by simply untying the piece of string and allowing the hinged portion to move slowly and evenly downwards and the traction weights need not be removed or the leg moved in any other way. It is possible to get further flexion by using a bed with a "cut-away" side. This method proved satisfactory in operation and the proper alignment of the fractured femur was not interfered with.

A man of 33 fell downstairs and sustained a fracture dislocation of C.5-C.6 with gross displacement. He was admitted a few hours later after an unsuccessful attempt at manual reduction. He had an almost complete paralysis of both upper limbs with sensory loss of whole right arm to pin and touch and loss of touch on left. Both legs were weak, loss of abdominal reflexes, dullness to pin-prick below D.9. Skull traction up to 40 lb. was applied. Catheterization was required once only, and lower limb recovery was fairly rapid. Reduction of the dislocation was completed by manipulation under traction at thirty-six hours. Wire and graft fixation at one week.

He was allowed up with a brace at six weeks. At this time he had gross hyperæsthesia and pain in the hands, worse on the right. The right arm had not completely recovered when the brace was discarded at three months.

At nine months after injury paralysis was almost completely recovered but with some residual stiffness of the right hand.

The X-ray showed full maintenance of position of C.5-C.6 with consolidation of the graft but there was a forward displacement of C.4-C.5 without symptoms. The significance of rupture of the interspinous ligament between C.4-C.5 was not appreciated at the time of operation.

The mechanism of production of fracture dislocations is either hyperflexion or compression or a combination of these two forces. Any marked degree of compression of the vertebral body is likely to be accompanied by fracture dislocation of the articular facets.

Fractures of the facets can sometimes but not always be seen, even in good X-rays. If present they may make reduction easy but also increase the liability to redisplacement.

Typically the upper vertebræ move forward on the lower, and the displacement is often unequal on the two sides so that a peculiar asymmetry of the neck and head can be seen on clinical examination. Study of this asymmetry is important, particularly during reduction. Forward displacement is not so obvious, as it can be partially concealed by motion at the occipito-atlantoid joint, and the patient is usually lying supine.

Attention has been drawn to the frequency with which cervical injuries are missed in the presence of head injuries due to falls. This is comparable to the combined os calcis and lumbar vertebra crush, and reminds us that compression injuries often affect more than one bone and require careful examination.

The neural injury in fracture dislocation of the spine is of two kinds. The cervical cord may be bruised or crushed, and the nerve roots emerging at the site of injury may be damaged. There is therefore often an "upper motor lesion" of the trunk and lower limbs, associated with a lower motor lesion of the cervical roots. The pain of the latter is often the patient's chief complaint.

True quadriplegias are more seldom seen in hospital because high lesions are often quickly fatal. The lesion of the cord often quickly extends upwards from the bony lesion, probably owing to œdema, but possibly by vascular damage, and death is frequently accompanied by hyperpyrexia.

Total interruption of conductivity of the cord is almost always a permanent and irremediable affair, but quite extensive paraplegias may show rapid recovery, particularly if any pressure on the cord can be relieved in a few hours. It is therefore essential that these injuries be treated as extreme emergencies. My cases of partial paraplegia have not required suprapubic cystotomy as the bladder function has returned in a few hours. Catheterization is not so dangerous in a recoverable lesion—it has been required on two occasions.

When cord symptoms are absent, reduction is not so urgent, but it is important where there are symptoms of root compression. Absence or failure of reduction

This transient increase of paraplegia with forward flexion of the head was also demonstrated in another case.

A man of 57 suffered a flexion injury from a fall. He was momentarily paralysed but resumed work.

Five years later he was admitted to hospital, having had increasing difficulty in walking for eighteen months due to weakness first in the right and later in the left leg—an X-ray showed gross forward dislocation of the atlas with fracture of the odontoid. There was spasticity of the legs and lumbar puncture showed a complete fluid block with the head flexed but relieved in extension. Occipito-axial fusion was performed under skull traction. The man died seven weeks after operation from cause apparently unrelated to the neck lesion.

Fractures of spinous processes of the cervical vertebræ in my experience have been confined to those produced by muscular action; the so-called "clay-shoveller's" fracture of the seventh cervical or first dorsal spinous process.

I have not met a case in a clay shoveller, but in a member of the Women's Land Army who was not sufficiently expert with a pitchfork. The failure of the clay to leave the shovel, or in my case the sheaf to leave the fork, fractures the spine by traction on the muscles.

These fractures usually fail to unite and persistent pain often leads to prolonged disability. Early excision of the separated spinous process is apparently the best treatment.

There has been one case in this series where a fracture of the lamina complicated a fracture dislocation, but I have not seen it as an isolated lesion.

Fractures of the bodies of the cervical vertebræ are usually of the compression or flexion type, and are frequently associated with dislocation, but I have seen one vertebral body split sagittally, which must have caused a considerable extradural hæmorrhage in the spinal canal, though no neurological symptoms were discovered.

I will now consider the more common type of fracture so often associated with dislocation.

Although severe bony damage is likely to be accompanied by severe cord injury, the severity of skeletal and neural damage does not run parallel and many cases have been described of severe neural damage in the absence of gross radiological changes. In these cases it must be presumed marked displacement of vertebræ must have occurred with rupture of ligaments and intervertebral disc, but the elasticity of the tissues restores the bones to a much more nearly normal position.

Now it is the integrity of the ligaments and disc upon which the stability of the cervical spine depends. It is the loss of this integrity which leads to the recurrence of the deformity which is so common, and the difficulty of its prevention was mentioned by Eastwood.

Nicoll has shown that when the intervertebral disc is injured in fractures of the spine its collapse is inevitable, and some angulation will persist however long the spine is immobilized in an over-corrected position.

I believe that this is also true of the cervical spine and dissent from Jefferson who apparently believed that prolonged traction would restore the integrity of the disc.

There is, however, another factor in the stability of the cervical spine, and that is the interspinous ligament.

Since I first noticed it I have found that in every case of fracture dislocation on which I have operated the interspinous ligament has shown signs of severe damage, or even complete rupture, and, what is very important, the damage is not always confined to the level of the dislocation but may also occur between the spines next above, so that a late deformity may appear at that level also.

A man of 33 fell downstairs and sustained a fracture dislocation of C.5-C.6 with gross displacement. He was admitted a few hours later after an unsuccessful attempt at manual reduction. He had an almost complete paralysis of both upper limbs with sensory loss of whole right arm to pin and touch and loss of touch on left. Both legs were weak, loss of abdominal reflexes, dullness to pin-prick below D.9. Skull traction up to 40 lb. was applied. Catheterization was required once only, and lower limb recovery was fairly rapid. Reduction of the dislocation was completed by manipulation under traction at thirty-six hours. Wire and graft fixation at one week.

He was allowed up with a brace at six weeks. At this time he had gross hyperæsthesia and pain in the hands, worse on the right. The right arm had not completely recovered when the brace was discarded at three months.

At nine months after injury paralysis was almost completely recovered but with some residual stiffness of the right hand.

The X-ray showed full maintenance of position of C.5-C.6 with consolidation of the graft but there was a forward displacement of C.4-C.5 without symptoms. The significance of rupture of the interspinous ligament between C.4-C.5 was not appreciated at the time of operation.

The mechanism of production of fracture dislocations is either hyperflexion or compression or a combination of these two forces. Any marked degree of compression of the vertebral body is likely to be accompanied by fracture dislocation of the articular facets.

Fractures of the facets can sometimes but not always be seen, even in good X-rays. If present they may make reduction easy but also increase the liability to redisplacement.

Typically the upper vertebræ move forward on the lower, and the displacement is often unequal on the two sides so that a peculiar asymmetry of the neck and head can be seen on clinical examination. Study of this asymmetry is important, particularly during reduction. Forward displacement is not so obvious, as it can be partially concealed by motion at the occipito-atlantoid joint, and the patient is usually lying supine.

Attention has been drawn to the frequency with which cervical injuries are missed in the presence of head injuries due to falls. This is comparable to the combined os calcis and lumbar vertebra crush, and reminds us that compression injuries often affect more than one bone and require careful examination.

The neural injury in fracture dislocation of the spine is of two kinds. The cervical cord may be bruised or crushed, and the nerve roots emerging at the site of injury may be damaged. There is therefore often an "upper motor lesion" of the trunk and lower limbs, associated with a lower motor lesion of the cervical roots. The pain of the latter is often the patient's chief complaint.

True quadriplegias are more seldom seen in hospital because high lesions are often quickly fatal. The lesion of the cord often quickly extends upwards from the bony lesion, probably owing to œdema, but possibly by vascular damage, and death is frequently accompanied by hyperpyrexia.

Total interruption of conductivity of the cord is almost always a permanent and irremediable affair, but quite extensive paraplegias may show rapid recovery, particularly if any pressure on the cord can be relieved in a few hours. It is therefore essential that these injuries be treated as extreme emergencies. My cases of partial paraplegia have not required suprapubic cystotomy as the bladder function has returned in a few hours. Catheterization is not so dangerous in a recoverable lesion—it has been required on two occasions.

When cord symptoms are absent, reduction is not so urgent, but it is important where there are symptoms of root compression. Absence or failure of reduction leads to a permanent deformity, usually of minor degree, but the cervical spine becomes stable in a few months, the damaged ligaments being replaced by scar tissue, and there is usually a rapid outgrowth from the front of the body below the lesion which supports and stabilizes the body of the vertebra above.

Motion is very little restricted as most of the movement of the neck occurs at the upper three joints.

In the absence of neural damage, therefore, reduction is not essential if it is contra-indicated by the age or condition of the patient. Protection of the injured spine in slight extension at first by sandbags, and subsequently by some form of cervical brace until stability is restored, is all that is required.

The late onset of symptoms due to cord injury is apparently uncommon. I know of two cases following cervical injury, though whether they were due to scarring of the cord or membranes or due to the pressure of a retropulsed disc, I cannot say. Symptoms of root pain may persist or appear late, particularly in unreduced lesions, and it is possible that root pains also may be due to a herniated disc.

In my opinion all dislocations should be treated at once, unless contra-indicated by the age and condition of the patient.

Reduction of nearly all dislocations can be achieved by manipulation or traction, open reduction being very rarely required, and I have no experience of it in the cervical spine. Reduction of dislocations can frequently be effected by manipulation, though I believe it to be a moderately dangerous procedure.

A child was brought to hospital with a history of a fall into a basement area on the previous day. Its mother stated that she found it with its neck twisted and flexed and pulled it straight. This was probably a unilateral dislocation reduced by unskilled traction. There was no resulting disability.

But in another case with a fracture dislocation of C.4-C.5 with minor C.N.S. symptoms, manipulation under anæsthesia failed to reduce the dislocation but considerably increased the degree of paralysis.

The man subsequently came under my care and recovered completely following skull traction, reduction and fixation by wire and graft.

The chief objection to manipulation, however, is the extreme difficulty of retaining position subsequently. The application of a Minerva jacket under such circumstances is a formidable task, its retention by the patient an ordeal, and the liability to re-displacement very great.

A youth of 18 injured his neck playing football. He was admitted twenty-four hours later with a dislocation of C.5-C.6. No fracture was seen. He had weakness of both hands and the right leg but no bladder paralysis. There was hyperæsthesia of the hands. With skull traction 40 lb. one facet unlocked and reduction was completed by manipulation under pentothal. A Minerva plaster was applied, but three months later while still in plaster redisplacement occurred, but without symptoms (figs. 1, 2 and 3). The spine was wired and grafted in the displaced position with a good functional result.

This case convincingly showed the unreliability of plaster fixation. It was subsequently proved that wiring the spinous process, under traction, to restore stability, and fixation by graft is a much more reliable method.

Traction by other than skeletal means is almost intolerable to the patient, and in my opinion is not justifiable. Skeletal traction may be applied to the cranial vault or the zygomatic arches. The application of hooks to the latter is easy and is probably the method of choice in the absence of special apparatus.

Traction on the cranial vault can be applied by the Blackburn apparatus or by stainless steel wire passed extradurally between two burr holes on either side of the skull. In all cases requiring traction I have used the Blackburn skull tractor.

Some details of the application of this apparatus may be worth recording. The object is to fix the flanges on the screws into the diploe between the two tables of the skull. The amount of diploe is very variable and is sometimes absent, particularly in the aged and very young.

The flanges may, if necessary, be placed against the inner table, i.e. extradurally, but, if so, the apparatus is only stable if both sides of the skull are treated in the same way.

The trephine holes should be symmetrically placed about 1½ in. vertically above the external meati below the parietal eminences. Traction must be vertical in relation to the skull. I have always used local anæsthesia for making the trephine holes as being safer. The wounds are sealed with collodion gauze. The patient having been placed supine on a Pearson bed head to foot of bed, 15 lb. of traction is applied to the skull tractor over a pulley with a check string in case of slipping. The bed is tilted so that the patient's body-weight is used as counter-traction. The patient's neck is not extended, in fact it may be very slightly flexed, which seems to help in unlocking of the facets. As soon as traction is applied, minor movements of the patient's head are not dangerous and his position is not uncomfortable.

Since seeing a young woman hanging from the roof of Olympia by her teeth, I have ceased to be frightened of traction, and rapidly increase the traction to 40 lb. or so, taking lateral X-rays at short intervals to observe the progress of distraction.

With adequate traction the facets may reduce themselves, but occasionally this occurs on one side only, producing the asymmetry of the neck previously mentioned.

When this occurs, manipulative reduction is easily accomplished under pentothal without releasing the traction. Gentle rotation of the head with slight lateral flexion to the appropriate side completes the reduction, sometimes with a palpable click, and the asymmetry disappears. If an X-ray confirms reduction, traction is immediately reduced to 15 lb. to allow the facets to engage normally while maintaining stability.

Even heavy traction is surprisingly painless and 15 lb. fairly comfortable. I have known unilateral subluxation where the facets were poised tip on tip, in which reduction occurred spontaneously with an audible snap under morphia without traction. Such an event cannot, of course, occur with a full dislocation.

Reduction having been accomplished, the next stage is to restore stability to the spine. Prolonged recumbency is tedious and uncertain. Immobilization in plaster is uncomfortable, difficult and insecure. Operative fixation is relatively easy, certain, and more satisfactory to the patient.

The patient, still under 15 lb. of traction, is transferred to the theatre and anæsthetized with an endotracheal tube, and placed in a prone position with his head supported on a rest.

The area having been prepared, the two vertebræ above and below the injury are exposed by a mid-line incision. The area is vascular, and a drip transfusion of a pint of blood may be advantageous.

On exposure one or more interspinous ligaments will be seen damaged. Abnormal mobility may be recognized at the site of the lesion which may also be located by identifying the spinous processes from the large and easily recognizable axis, or by a lateral X-ray with a metal marker on one of the spines. A stainless steel wire on an aneurysm needle is now passed beneath an undamaged interspinous ligament round a spine above the lesion and back caudal to a spine below the lesion, and the two ends are then tied at the side. As the wire is tightened, the head traction is released.

This replacement of the interspinous ligament by wire immediately produces a marked increase in the stability of the spine, and allows the rest of the operation to be conducted with safety.

One word of warning—the spinous process of the third cervical vertebra is a miserable thing, and it is better to put a wire round the spine of the axis than to trust to it (figs. 4, 5 and 6).

leads to a permanent deformity, usually of minor degree, but the cervical spine becomes stable in a few months, the damaged ligaments being replaced by scar tissue, and there is usually a rapid outgrowth from the front of the body below the lesion which supports and stabilizes the body of the vertebra above.

Motion is very little restricted as most of the movement of the neck occurs at the upper three joints.

In the absence of neural damage, therefore, reduction is not essential if it is contra-indicated by the age or condition of the patient. Protection of the injured spine in slight extension at first by sandbags, and subsequently by some form of cervical brace until stability is restored, is all that is required.

The late onset of symptoms due to cord injury is apparently uncommon. I know of two cases following cervical injury, though whether they were due to scarring of the cord or membranes or due to the pressure of a retropulsed disc, I cannot say. Symptoms of root pain may persist or appear late, particularly in unreduced lesions, and it is possible that root pains also may be due to a herniated disc.

In my opinion all dislocations should be treated at once, unless contra-indicated by the age and condition of the patient.

Reduction of nearly all dislocations can be achieved by manipulation or traction, open reduction being very rarely required, and I have no experience of it in the cervical spine. Reduction of dislocations can frequently be effected by manipulation, though I believe it to be a moderately dangerous procedure.

A child was brought to hospital with a history of a fall into a basement area on the previous day. Its mother stated that she found it with its neck twisted and flexed and pulled it straight. This was probably a unilateral dislocation reduced by unskilled traction. There was no resulting disability.

But in another case with a fracture dislocation of C.4-C.5 with minor C.N.S. symptoms, manipulation under anæsthesia failed to reduce the dislocation but considerably increased the degree of paralysis.

The man subsequently came under my care and recovered completely following skull traction, reduction and fixation by wire and graft.

The chief objection to manipulation, however, is the extreme difficulty of retaining position subsequently. The application of a Minerva jacket under such circumstances is a formidable task, its retention by the patient an ordeal, and the liability to re-displacement very great.

A youth of 18 injured his neck playing football. He was admitted twenty-four hours later with a dislocation of C.5-C.6. No fracture was seen. He had weakness of both hands and the right leg but no bladder paralysis. There was hyperæsthesia of the hands. With skull traction 40 lb. one facet unlocked and reduction was completed by manipulation under pentothal. A Minerva plaster was applied, but three months later while still in plaster redisplacement occurred, but without symptoms (figs. 1, 2 and 3). The spine was wired and grafted in the displaced position with a good functional result.

This case convincingly showed the unreliability of plaster fixation. It was subsequently proved that wiring the spinous process, under traction, to restore stability, and fixation by graft is a much more reliable method.

Traction by other than skeletal means is almost intolerable to the patient, and in my opinion is not justifiable. Skeletal traction may be applied to the cranial vault or the zygomatic arches. The application of hooks to the latter is easy and is probably the method of choice in the absence of special apparatus.

Traction on the cranial vault can be applied by the Blackburn apparatus or by stainless steel wire passed extradurally between two burr holes on either side of the skull. In all cases requiring traction I have used the Blackburn skull tractor.

Two laminæ above and below the lesion on either side are now roughened with an electric burr and two tibial grafts of equal and appropriate length with holes drilled near their ends are fixed in position with a wire in a somewhat similar manner to the first wire. Secure fixation is easily attained, the grafts lying under the overhanging bifid spines (figs. 7 and 8).

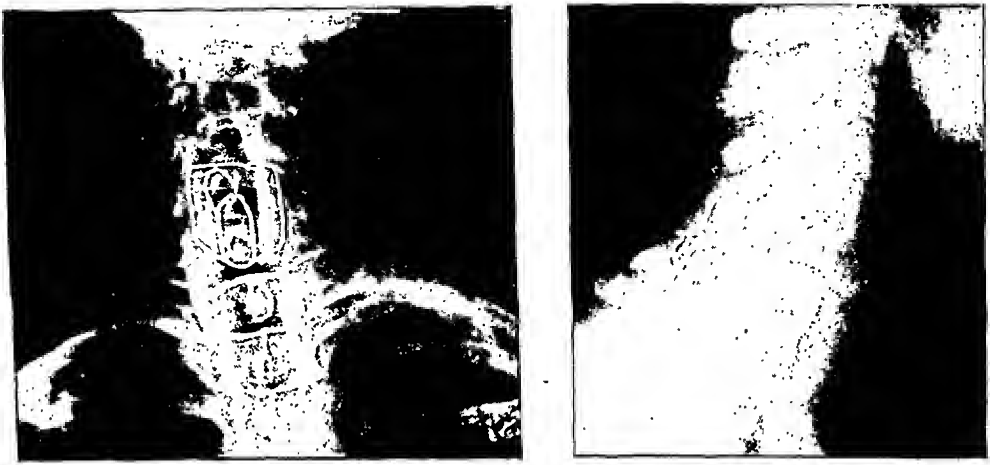


FIG. 7. FIG. 8.

FIGS. 7 and 8.—Stainless steel wire round spinous processes replacing damaged interspinous ligament and restoring stability. Two tibial grafts wired into position.

The wound is now closed and the skull tractor removed. The patient is kept supine in bed for two to three weeks and then fitted with a cervical brace and allowed up. The brace is retained for three months, by which time the X-ray usually shows consolidation of the grafts (figs. 9 and 10).

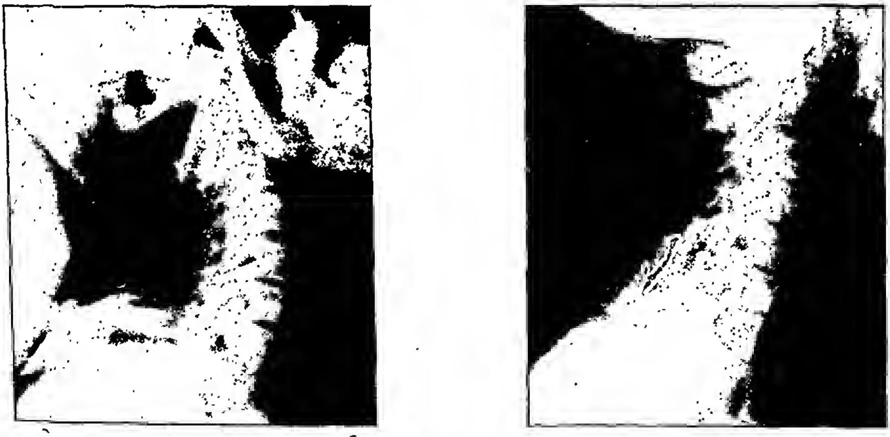


FIG. 9. FIG. 10.

FIGS. 9 and 10.—Consolidation of grafts after six months.

By this method the patient is not confined to bed for more than a month, no massive plaster jacket is required, and the danger of redisplacement is minimized. Very little

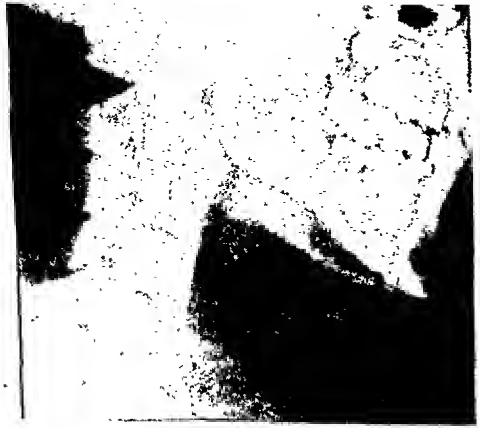


FIG. 1.

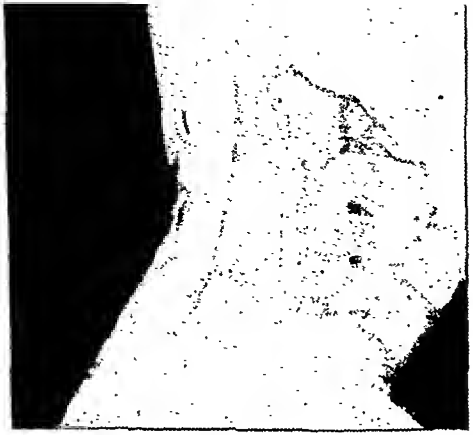


FIG. 2.

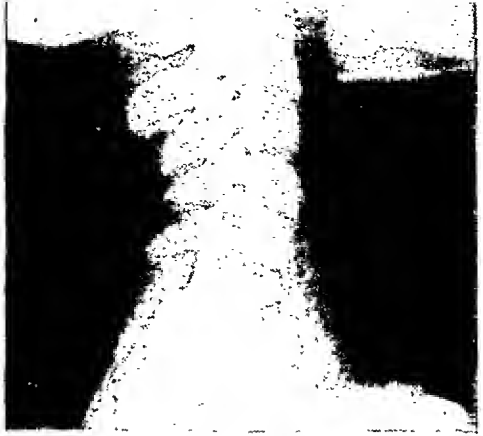


FIG. 3.

FIGS. 1, 2, 3.—Fracture dislocation C.5-C.6; reduction and immobilization followed by recurrence.

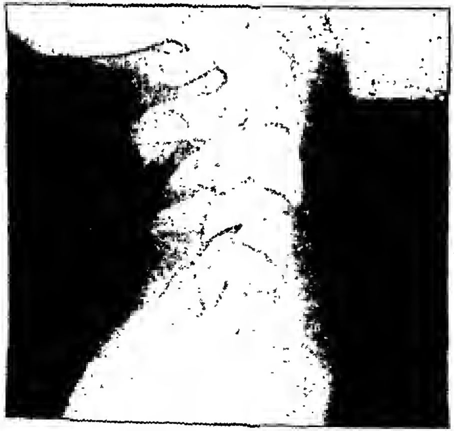


FIG. 4.

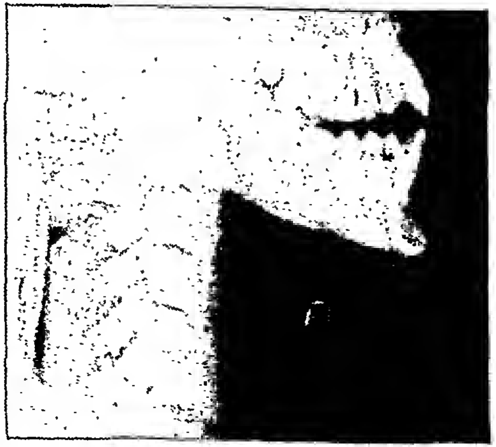


FIG. 5.

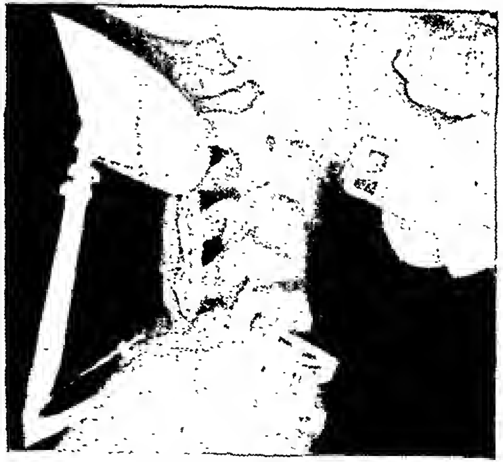


FIG. 6.

FIGS. 4, 5, 6.—Fracture dislocation C.4-C.5 from dive into shallow water; wiring and grafting C. 3, 4, 5, 6. small spine of C.3.

Recurrence of displacement due to wire slipping off

Section of Experimental Medicine and Therapeutics

President—Professor H. P. Himsworth, M.D.

[*October* 8, 1946]

Protein Metabolism in Relation to Disease

PRESIDENT'S ADDRESS

By Professor H. P. Himsworth, M.D.

Although only some twenty-two amino-acids are available for the construction of all varieties of protein, no two proteins are alike. Not only do those of the different tissues differ from each other but there are subtle species differences between the proteins of the same organ. The tissue differences can be referred, at least in part, to differences in their amino-acid composition; those of the skin, for example, being particularly rich in cystine, those of the wheat germ in glutamic acid. In one instance a species difference has been referred to a similar difference in composition, it having been found that cows' milk contains more arginine, tryptophan and sulphur-containing amino-acids than human milk (Williamson, 1944). But, as yet, most species differences are too subtle for detection by chemical analysis and recourse must be had to immunological tests. It would, however, be unjustifiable to assume that all differences between proteins are referable either to the proportions or arrangement of the various amino-acids within the molecule. The classical researches on the pneumococcal antigens have clearly shown that the protein moiety is common to all these and that the specificity of the different types is dependent upon a characteristic polysaccharide. More recently lipoproteins have been distinguished (Cohn *et al.*, 1944), and it may well be that, with the development of more delicate methods of separating proteins, species, and perhaps even tissue, differences dependent upon such attached substances may be revealed. Nevertheless the myriads of different proteins formed in Nature are each characteristic and remain true to type. Alterations in the quantity or quality of the dietary protein may influence the amount of the different tissue proteins formed, but they will not apparently induce the body to form imperfect or unusual protein molecules.

This well-established specificity of the different tissue proteins has very naturally led to the tacit assumption that the proteins in the tissues are in a comparatively stable state and to be regarded more as structural elements than as participants in the stream of metabolism on the same plane of activity as carbohydrates and fats. Against the background of this view Folin put forward the conception of endogenous and exogenous metabolism. According to this endogenous protein metabolism was the result of the breakdown through wear and tear of the actual tissues of the body. Exogenous protein metabolism, on the other hand, represented the burning off of the excess of the amino-acids, derived from the dietary protein, after the tissues had abstracted those required for their repair. These views now appear to be mistaken. Far from being stable structures the proteins of the different tissues are constantly undergoing rapid change. Amino-acids pass from one protein molecule to another not only in the same, but between different tissues. Individual amino-acids are constantly being broken down and the fragments built up either into similar or different amino-acids. When protein is ingested the resulting amino-acids are swept into this whirl of activity and can in no way be distinguished, either by situation or stability, from those already present in the tissues (Schoenheimer, 1942). The limitation of motion has followed in any case, and at least two are serving in the Army, Category A.

The third stage of treatment is really only necessary in those cases which have had neural symptoms. As already mentioned, the incomplete paraplegia rapidly recovers and no disability in the legs remains after a month or so of exercises.

The recovery from root symptoms in the arms is often much more difficult. The severe pain and hyperæsthesia in the arms makes the task of the physiotherapist in restoring the wasted muscles difficult, and it is very unpleasant for the patient. It may be very difficult to prevent the finger-joints from becoming stiff if the patient cannot bear to be touched. Fortunately, the nerve lesion is usually a neurapraxia, and recovers rapidly but in one of our cases a minor permanent weakness persists.

FRACTURE DISLOCATIONS OF THE CERVICAL SPINE.

Plan of Treatment in Early Cases of Unreduced Dislocations.

(1) Skull traction using Blackburn skull tractor. Local anæsthetic. Suprapubic cystostomy at the same time if required.

(2) Traction increased as necessary up to 40 lb. in course of twenty-four to forty-eight hours on reversed Pearson bed. Frequent check lateral X-rays.

(3) If unreduced by traction manipulate under pentothal in bed on traction. (Done in 3 unilateral cases.)

(4) At seven to ten days wire and graft cervical spine above and below lesion Localizing X-ray. Traction continuing until wires are tightened.

(5) Bed with head between sandbags for three weeks.

(6) Up wearing cervical brace for three to four months.

FRACTURE DISLOCATIONS CERVICAL SPINE.

Total number of cervical spine injuries	34
Number of fracture dislocations	20

Average age 37. Oldest 65. Youngest 16.

	No. of Cases.	
Admitted within 24 hours	8	
Admitted late	12	(5 years, 7, 6, 3, 2, 2, 1, 1 months 2, 2, 2, 2 weeks)
With cord symptoms	10	
With root symptoms only	4	
No neurological symptoms	6	
Fused	14	
Died	3	
Returned to work or duty	12	
Under treatment	2	
Not known	3	

Level of fracture dislocation, cervical spine.	
1/2	1
2/3	0
3/4	2
4/5	5
5/6	6
6/7	6

soldiers, when many races subsist on much smaller amounts. Long ago Chittenden maintained that intakes of ¼ to ⅓ gramme of protein per kilo sufficed for adults and certainly limitation of dietary protein short of starvation does not bring growth to a standstill or prevent the inception of lactation or the production of an apparently normal fœtus. The question, however, is one not of absolute adequacy or inadequacy, but of optimal or suboptimal nutrition. Comparison of races living on high with those living on low protein diets reveals that the former have better physique, more energy and better health than the latter (Cuthbertson, 1940). Recent studies in Holland have shown that when the supply of protein is minimal, lactation can be established, and milk of normal composition obtained, but lactation cannot be maintained. Observation in the East on races taking low protein diets revealed that, while the diet appeared adequate under ordinary conditions, additional strain such as pregnancy (Upadhyay, 1944) or infection, precipitated illnesses which either did not occur, or appeared only in a mild form, in races taking larger amounts of dietary protein.

Therefore, although under ordinary circumstances gross restrictions of dietary protein are necessary to produce illness, much lighter restrictions may allow such illnesses to appear under strain. Such strains are growth, pregnancy, infection, injury and surgical operations. Both physicians and surgeons would do well to bear this in mind when devising pre-operative treatment or supportive measures.

Biologically speaking the individual amino-acids fall into two groups according to whether they must or need not, be supplied in the diet. These groups are called respectively the essential and the non-essential amino-acids. There is a possibility of a misconception arising from this terminology. By the use of tracer elements it has been shown that all the amino-acids, with the possible exception of lysine, can be synthesized within the body, either from the chemical groupings in other amino-acids or from simpler materials (Schoenheimer, 1942). Apparently, however, the rate of production of ten of the amino-acids is too slow for the needs of the body so that, if normal nutrition is to be maintained, supplementary quantities must be supplied in the food. These have, therefore, come to be regarded as the essential amino-acids but it would be quite unjustifiable to regard the remaining dozen or so of such acids as optional substances which may or may not be incorporated in the body proteins. It may well be that in the future we shall discover conditions in which the demand for an amino-acid, now considered unessential, outstrips its production. Under such circumstances, that amino-acid would be upgraded to the essential category. It is not even certain that all those amino-acids now called essential are always so. Their reputation as such is largely based upon their being necessary for growth and for this threonine, tryptophan, methionine, leucine, isoleucine, valine, lysine, phenylalanine, histidine and arginine are indispensable (Rose, 1938). But only the first six appear necessary for the maintenance of the adult rat and phenylalanine can be replaced by tyrosine (Burroughs, Burroughs and Mitchell, 1940; Mitchell, 1942). These findings have been confirmed for human adults (Rose *et al.*, 1943), and the indispensability of methionine, threonine, isoleucine and leucine established. There is even evidence that, in protein-depleted men, administration of the ten amino-acids will promote the formation of more protein than intact protein itself (Emerson and Binkley, 1946). The quantitative requirements of healthy men for the different amino-acids have not yet been ascertained but data are available on the approximate amounts of twelve of these in a diet adequate to maintain health (Melnick, 1943). It is evident, however, that the requirements differ both qualitatively and quantitatively, at the various stages of development.

Closely connected with the question of essential amino-acids is the conception of "key" amino-acids. When an essential amino-acid is removed from the diet then breakdown of protein is accelerated so that more nitrogen is excreted in the urine proteins of the body are boiling with activity yet their characteristics and the structure of the tissues they compose, are preserved in a dynamic equilibrium. Astounding as is this new view it does indicate the explanation of one problem, namely that of "labile body protein".

It has long been known that when a starved animal is fed it retains a significant proportion of the ingested protein and that, on starving the animal again, protein to the amount retained is broken down. Under the old view of endogenous and exogenous protein metabolism such protein should have been stored, just like fat in adipose tissue or glucose as glycogen. But no such stores could ever be demonstrated. All that could be seen was that certain cells, such as the liver parenchyma, enlarged on repletion and shrank on starvation. But their chemical composition as regards protein remained the same. According to the new view the amino-acids from ingested protein are incorporated into the tissues as components of the characteristic proteins of the body. The mass of living protoplasm in the body thus becomes adjusted to the intake of protein. Decrease this and the tissues of the body itself, not hypothetical stores of protein, begin to waste. That is the significance of a nitrogen excretion greater than the intake; that is why such a negative nitrogen balance in illness cannot lightly be dismissed.

REQUIREMENTS FOR PROTEIN AND AMINO-ACIDS

A distinction must be drawn between the requirements for a particular protein, when this constitutes the sole or main source of amino-acids, and the requirements for the mixture of proteins in a normal diet. The former is dependent upon the amino-acid composition of the particular protein and is of practical importance only when the protein intake is low either because of illness or shortage of dietary protein. The requirement for mixed protein is, in health and with normal food supplies, largely independent of such considerations for differences in the amino-acid composition of the numerous proteins in a normal diet compensate each other so that the mixture as a whole has an adequate biological value (Macrae, Henry and Kon, 1943). It is, therefore, possible to consider separately the requirements for proteins in general and the requirements for individual amino-acids in particular.

The requirements for protein in general have largely been determined in reference to growth and the maintenance of weight, and the conclusions drawn from such studies are only valid when considered in relation to the intake of other dietary substances. When protein is the sole food it has to provide not only material for the construction of body tissues but also fuel for their working. Under such conditions the amounts required to promote growth or maintain weight are necessarily large. But, when the diet contains other adequate sources of fuel, ingested protein can largely be devoted to its proper purpose, and of such energy foods carbohydrate is the most efficient "protein sparer" (Lusk, 1917). This point becomes important when, as in illness, the food intake is low and it is necessary to obtain the maximum benefit from the limited intake of protein which is possible. In ordinary circumstances, however, it can largely be disregarded for, when food supplies are adequate, the natural choice ensures a dietary comprising adequate amounts of energy foods. Then the special problems of protein requirements in health are reduced to determining the extra requirements for growth, pregnancy and lactation. Taking the requirements for adults as the standard the consensus of opinion is that this is of the order of 1 gramme of protein per kilo of body-weight daily. In children, however, 3 grammes/kilo is necessary and intermediate amounts in pregnancy and lactation (McCollum, Orent-Keiles and Day, 1939). Details of these different requirements are given in the Table constructed by Cuthbertson (1944) from the most recent figures on the subject.

It may well be asked what is the justification for such liberal allowances of protien, and the even higher intakes sanctioned by tradition for such special categories as soldiers, when many races subsist on much smaller amounts. Long ago Chittenden maintained that intakes of ¼ to ⅓ gramme of protein per kilo sufficed for adults and certainly limitation of dietary protein short of starvation does not bring growth to a standstill or prevent the inception of lactation or the production of an apparently normal fœtus. The question, however, is one not of absolute adequacy or inadequacy, but of optimal or suboptimal nutrition. Comparison of races living on high with those living on low protein diets reveals that the former have better physique, more energy and better health than the latter (Cuthbertson, 1940). Recent studies in Holland have shown that when the supply of protein is minimal, lactation can be established, and milk of normal composition obtained, but lactation cannot be maintained. Observation in the East on races taking low protein diets revealed that, while the diet appeared adequate under ordinary conditions, additional strain such as pregnancy (Upadhyay, 1944) or infection, precipitated illnesses which either did not occur, or appeared only in a mild form, in races taking larger amounts of dietary protein.

Therefore, although under ordinary circumstances gross restrictions of dietary protein are necessary to produce illness, much lighter restrictions may allow such illnesses to appear under strain. Such strains are growth, pregnancy, infection, injury and surgical operations. Both physicians and surgeons would do well to bear this in mind when devising pre-operative treatment or supportive measures.

Biologically speaking the individual amino-acids fall into two groups according to whether they must or need not, be supplied in the diet. These groups are called respectively the essential and the non-essential amino-acids. There is a possibility of a misconception arising from this terminology. By the use of tracer elements it has been shown that all the amino-acids, with the possible exception of lysine, can be synthesized within the body, either from the chemical groupings in other amino-acids or from simpler materials (Schoenheimer, 1942). Apparently, however, the rate of production of ten of the amino-acids is too slow for the needs of the body so that, if normal nutrition is to be maintained, supplementary quantities must be supplied in the food. These have, therefore, come to be regarded as the essential amino-acids but it would be quite unjustifiable to regard the remaining dozen or so of such acids as optional substances which may or may not be incorporated in the body proteins. It may well be that in the future we shall discover conditions in which the demand for an amino-acid, now considered unessential, outstrips its production. Under such circumstances, that amino-acid would be upgraded to the essential category. It is not even certain that all those amino-acids now called essential are always so. Their reputation as such is largely based upon their being necessary for growth and for this threonine, tryptophan, methionine, leucine, isoleucine, valine, lysine, phenylalanine, histidine and arginine are indispensable (Rose, 1938). But only the first six appear necessary for the maintenance of the adult rat and phenylalanine can be replaced by tyrosine (Burroughs, Burroughs and Mitchell, 1940; Mitchell, 1942). These findings have been confirmed for human adults (Rose *et al.*, 1943), and the indispensability of methionine, threonine, isoleucine and leucine established. There is even evidence that, in protein-depleted men, administration of the ten amino-acids will promote the formation of more protein than intact protein itself (Emerson and Binkley, 1946). The quantitative requirements of healthy men for the different amino-acids have not yet been ascertained but data are available on the approximate amounts of twelve of these in a diet adequate to maintain health (Melnick, 1943). It is evident, however, that the requirements differ both qualitatively and quantitatively, at the various stages of development.

Closely connected with the question of essential amino-acids is the conception of "key" amino-acids. When an essential amino-acid is removed from the diet then breakdown of protein is accelerated so that more nitrogen is excreted in the urine than is ingested in the food. Certain proportions of all the amino-acids are required in the construction of most tissue proteins. If one is missing the protein cannot be constructed and the remaining amino-acids are rapidly burnt off. The missing amino-acid is thus in the position of a limiting factor, a "key" component, in protein synthesis and wastage will continue until it is supplied in sufficient amounts.

THE PRODUCTION OF PROTEIN DEFICIENCY

Deficiency states occur when the demand for a nutrient exceeds its supply. It is thus possible to produce protein deficiency either by curtailing the amount of protein entering the body or, such amounts being normal, by increasing its utilization or loss from the body. Theoretically supplies may be restricted because of inadequate diet or conditions of the alimentary tract such as anorexia, failure of digestion or absorption. Excessive utilization occurs in pregnancy, fevers, in metabolic diseases like diabetes mellitus, and after injury or operation; excessive loss in renal lesions or conditions, such as burns, where body fluids escape.

Dietary deficiency confined to protein does not ordinarily occur in Western civilizations for, with remarkable regularity, the dietary habits of such countries ensure that, whatever the calory value of the diet, protein supplies 10 to 12% of the calories. It is not so elsewhere. Many Eastern races take diets containing less than the minimum of protein and live habitually in a state which in Europe is only seen in times of famine. Under these circumstances the order of development of the clinical states referable to dietary deficiencies is largely determined by the ability of the body to store different foodstuffs. Energy foods can be stored in quantity; protein and most vitamins to only a limited extent. In famine, therefore, protein deficiency, with or without vitamin deficiencies, dominates the clinical picture.

Under normal conditions in Western civilizations protein deficiency states usually occur secondary to some illness. This may be a structural lesion of the alimentary tract, such as a carcinoma of the œsophagus, which bars access of food to the gut; a gastro-colic fistula, which short circuits food past the small intestine; or an operative procedure on the gut itself. On the other hand, the illness may be a disturbance of function.

Anorexia is a common cause of latent, and more rarely of manifest, protein deficiency. It may arise from mental causes, as in anorexia nervosa, or lesions in the alimentary tract such as alcoholic gastritis. But it has only recently been realized that protein deficiency itself produces anorexia and that this is related to the absence of particular amino-acids. Thus, in the absence of methionine the food intake of rats falls to very low levels. Addition of a few milligrammes of this substance restores the appetite to normal although the amount in the diet is still insufficient to meet other requirements. The addition of the other sulphur-containing amino-acid, cystine, is, however, of no benefit (Glynn, Himsworth and Neuberger, 1945). A vicious cycle is thus set up by anorexia and this may explain the disappearance of appetite on starvation and the common clinical observation that, once a case of anorexia nervosa has been forced to eat, appetite may rapidly return.

Failure to digest dietary protein into amino-acids would, if it occurred, be a potent cause of protein deficiency and according to tradition such a failure occurs in extreme starvation. But little evidence in support of this view has been obtained in modern studies on starvation. What has been obtained, however, is evidence that absorption of amino-acids from the gut is retarded in starved patients who suffer also from diarrhœa. At Belsen camp there were many such patients and hydrolysed casein given to them by mouth passed through the gut and appeared as a solution of amino-acids in the diarrhœic stools (Dent, Pitt-Rivers and Vaughan, 1945). It cannot, therefore, be assumed that benefit will accrue from the oral administration of pre-digested protein to cases of diarrhœa and, indeed, observations on the above patients suggest that the preparations then available had no advantage over skim milk powder. It is, however, likely that in profuse small intestinal diarrhœa, such as occurs in typhoid fever or regional ileitis, much ingested protein may be lost and parenteral administration of suitable protein may be the only effective way of restoring the nutrition of such cases.

Specific amino-acid deficiencies can rarely, if ever, arise from a general shortage of protein, whether produced directly or indirectly. They may, however, arise secondary to other causes. A poison may react with a particular amino-acid, producing a substance inutilizable in metabolism, and thus lead to a conditioned amino-acid deficiency.

HYPOPROTEINÆMIA

The maintenance of a normal level of protein in the plasma requires the ingestion of adequate dietary protein. Not all protein foods are equally useful (Madden and Whipple, 1940; Whipple, 1942). Beef serum is five times as effective as beef stomach and there is some evidence that, under certain conditions, sulphur-containing amino-acids occupy a key position in the synthetic process (Whipple, 1942; Glynn, Himsworth and Neuberger, 1945). Plasma albumin, together with the two globulins, fibrinogen and prothrombin, are apparently formed in the liver. The source of the remaining plasma globulins is not certain but the association of hyperglobulinæmia with proliferation of the reticulo-endothelial system suggests that they may originate in that tissue. Arising from different sources, and varying so independently in disease, there would seem to be as little theoretical justification as there is clinical value in the common practice of expressing the state of the plasma proteins by the albumin-globulin ratio.

Of the plasma proteins albumin is most susceptible to abnormal conditions. In starvation, either direct or indirect, it falls relatively quickly while plasma globulin is affected little if at all. Owing to the small size of its molecule it readily escapes from the blood when capillary permeability is increased as happens in the renal glomerulus in nephritis. It is apparently synthesized more slowly than the globulins and even mild liver damage is sufficient to retard this synthesis. But despite the different origin of albumins and most globulins the levels of one in the plasma is not without influence on the other. If the protein intake is satisfactory, yet hypo-albuminæmia develops either from loss or deficient synthesis, then slowly the plasma globulin concentration increases until the total concentration of protein in the plasma may equal, or even surpass, the normal level. The reason for this increase is not clear but it, at least, serves a useful purpose in raising the reduced colloidal osmotic tension of the blood.

Œdema is the most striking objective manifestation of hypoproteinæmia, and commonly appears when the total plasma protein level falls below 4·5 to 5 grammes/100 c.c. It is, however, more closely correlated with the albumin fraction and this is to be expected as albumin contributes most to the colloidal osmotic tension of the blood. Whether the fall is produced by deficient formation, as in starvation and liver disease, or by depletion, as in nephrosis or exudation, if the plasma albumin falls below 3 grammes/100 c.c. œdema appears (Bruckman and Peters, 1930) only to disappear when the level is restored by transfusion of albumin (Thorn, Armstrong and Davenport, 1946). Hypoproteinæmia, however, only predisposes to œdema. Adequate amounts of water and salt are required for its formation. Dehydration, therefore, from any cause may prevent its development so that œdema may only appear in the course of treatment when fluid is restored to the body. This has been a common experience in the treatment of hunger œdema complicated by dysentery and, in civil practice, accounts for the œdema which may develop in wasted diabetics after the polyuria is controlled by insulin. It is, however, doubtful whether all cases of famine œdema can be explained on these lines. Some can (Leyton, 1946) and hypoproteinæmia probably plays its part in most. But under conditions of famine other deficiencies are present and indications have been obtained that these may introduce another factor, probably that of increased capillary permeability (Keys, Taylor, Mickelsen and Henschel, 1946).

The plasma proteins occupy a peculiarly important position in relation to protein metabolism for their level in the blood depends upon the protein content of the body tissues in general. It is a common clinical observation that, when blood transfusions of ordinary size are given to hypoproteinæmic patients, the added plasma proteins rapidly leave the circulation although the blood corpuscles remain behind. Considerable light has been thrown upon the significance of this phenomenon by experiments upon dogs made hypoproteinæmic by dietary deficiency. These showed that 30 grammes of albumin had to be retained in the body to secure an increase of 1 gramme in the circulation, and conversely that to lower the total circulating albumin by 1 gramme the body had to be depleted of 30 grammes (Sachar, Horvitz and Elman, 1942). Evidently an equilibrium is maintained between plasma albumin and tissue protein and that this has a nutritional significance is shown by the observation that it is possible to keep dogs in nitrogen equilibrium when transfusions of plasma are the sole source of protein. Applying these results to a man of average size it will be seen that a fall in plasma albumin concentration of 1 gramme/100 c.c. implies a loss of protein to the body of over 1 kilo, the amount contained 4 kilo of muscle. A fall of plasma albumin concentration should not, therefore, be regarded lightly for in all cases it is diagnostic of a far greater depletion of body protein.

INJURY, FEVER AND CONVALESCENCE

In febrile illnesses there is an excessive breakdown of body protein. Associated with this is a raised basal metabolic rate (Du Bois, 1936). The destruction of protein is due neither to the raised metabolism nor to the fever for the protein breakdown in fever is greater than in normal subjects whose metabolism has been elevated to the same degree by exercise (Kocher, 1914), and is not augmented in pyrexias induced by external temperature (Graham and Poulton, 1912-13). It is apparently referable to some unknown process initiated by the illness itself which has been loosely termed "toxic destruction". If this term is taken to imply a process due to an extrinsic toxin it is probably a misnomer for Cuthbertson (1928) has demonstrated that a similar destruction and elevation of the metabolic rate occurs after injury even when this is of a relatively minor character. This finding has been confirmed after fractures, dislocations, burns and surgical operations (Cuthbertson, 1945) and it now seems evident that the process is a reaction of the body itself. The sequence of events seems to be the same in each case but can be studied in its simplest form after a single injury. Shortly after injury the nitrogen breakdown begins to increase and reaches its maximum on the second to eighth day. It then sinks back to normal in a week or ten days and thereafter the phase of convalescence follows which may last for several weeks, and in which more protein is stored than is destroyed. Finally the body again comes into nitrogen equilibrium and excretion equals intake.

The relationship of dietary protein to this train of events is of importance. In the stage of active breakdown the loss can be mitigated by increasing the intake of protein but it can rarely be prevented entirely even by enormous amounts of dietary protein. As the rate of breakdown diminishes, however, it becomes correspondingly easy to promote retention of protein by augmenting the intake and, in the convalescent phase, the deficit may be rapidly replaced, and the duration of this phase shortened, by dietary measures. The degree of protein breakdown is influenced by two further factors. It is increased when atrophy consequent upon inactivity is allowed to occur; when the previous nutrition is poor it may be absent.

The significance of this reaction is not yet clear. The excessive excretion of nitrogen in the first ten days after a simple fracture may be equivalent to 8% of the total body protein, that is about four times the total protein content of the liver. If this large loss were a local event, confined to the region of the injury, it could not escape detection. The excessive protein destruction seems to involve the body tissues as a whole and the associated excessive excretions of phosphorus and sulphur indicate that it is largely derived from muscle. Cuthbertson (1932) has suggested that the purpose of this generalized breakdown of body protein is to provide large amounts of amino-acids necessary for repair, and so render the healing process independent of the intake of dietary protein. Implicit in this suggestion is the idea that certain key amino-acids are in great demand and that the excessive excretion of nitrogen arises from the destruction of the excess of other amino-acids which are less urgently required in the repair process but which are simultaneously released when body protein is broken down. In support of this suggestion is the observation that dietary supplements of methionine reduce conspicuously the excretion of nitrogen following experimental burns (Croft and Peters, 1945). Of the mechanism initiating such protein destruction there is no certain knowledge. That it can be influenced by endocrine factors has been shown (Cuthbertson, Shaw and Young, 1941; Josiah Macy Foundation Report, 1942), but that these are responsible for the actual event has not been established.

The practical importance of these observations has not yet been fully realized. It seems probable that loss of body proteins is responsible for the wasting and cachexia, termed "wound phthisis" (Rusakow, 1943) which follows infected injuries. It may well underlie the "toxic anæmia" of chronic infections and those following burns. It may be the reason why Eastern troops, on low protein diets, as compared with white troops on adequate protein diets, show more physical deterioration, more complications like anæmia and require protracted convalescence, after injury or infection. These points require further investigation but the immediate practical indications are clear. Before operation any depletion of the protein stores of the body should be remedied. In the acute stage of short illnesses, or for the first few post-operative days, the intake of protein should be maintained at reasonable levels but, as most will be destroyed, metabolism need not be overloaded by forcing it to high levels. In protracted illnesses, however, every gramme of protein prevented from destruction counts and the protein intake should be maintained if necessary by parenteral feeding. But as soon as improvement appears the level of intake should be forced up and thereafter, and throughout convalescence, should not fall below 150 grammes daily. Statistical evidence that such measures are of practical value is difficult to assess but clinical impression of the increased well-being which results when these principles are acted upon justifies their adoption in practice.

ANÆMIA

The work of Whipple and his school (Madden and Whipple, 1940; Whipple, 1942) has clearly established that the production of hæmoglobin is dependent upon the quality and quantity of the dietary protein. In recent years increasing evidence has accumulated that tropical macrocytic anæmia is of dietary origin and in particular may be associated with deficiency of dietary protein (Wills and Mehta, 1929-30; Wills, 1933-34; Wills and Evans, 1938; Trowell, 1942, 1943; Upadhyay, 1944; Taylor and Chhuttani, 1945). Experimentally deficiency of the essential amino-acids lysine (Harris, Neuberger and Sanger, 1943), phenylalanine (Maun, Cahill and Davis, 1945) or methionine (Glynn, Himsworth and Neuberger, 1945) has been shown to produce anæmia and, in the case of methionine deficiency, this anæmia has been demonstrated to have the same morphological characteristics as tropical macrocytic anæmia. The work in this field has hardly begun, even in relation to tropical diseases where it would seem to be most relevant, but one significant point has already been demonstrated. It has been shown (Upadhyay, 1944) that an intake of protein, sufficient to prevent anæmia in the non-pregnant woman, is insufficient when she is pregnant. That protein deficiency may play a part in the anæmias following infection or injury has already been suggested. It may also be of importance in the anæmias following exposure to such poisons as trinitrotoluene which are known to combine with amino-acids.

BIBLIOGRAPHY

BERMAN, C. (1935) *S. African J. med. Sci.*, **1**, 12.
BRUCKMAN, F. S., and PETERS, J. P. (1930) *J. clin. Invest.*, **8**, 591.
——, D'ESOPO, L. M., and PETERS, J. P. (1930) *J. clin. Invest.*, **8**, 577.
BURROUGHS, E. W., BURROUGHS, H. S., and MITCHELL, H. H. (1940) *J. Nutrit.*, **19**, 363 and 385.
CANNON, P. R., CHASE, W. E., and WISSLER, R. W. (1943) *J. Immunol.*, **47**, 133.
COHN, E. J., ONCLEY, J. L., STRANG, L., HUGHES, W. L., and ARMSTRONG, S. H. (1944) *J. clin. Invest.*, **23**, 417.
CONNOR, C. L. (1938) *Amer. J. Path.*, **14**, 347.
CROFT, P. B., and PETERS, R. A. (1945) *Lancet* (i), 266.
CURTIS, A. C., and NEWBURGH, L. H. (1927) *Arch. intern. Med.*, **39**, 828.
CUTHBERTSON, D. P. (1928) *Biochem. J.*, **23**, 1328.
—— (1932) *Quart. J. Med.*, **25**, 233.
—— (1940) *Nutrit. Abstr. and Rev.*, **10**, 1.
—— (1944) *Brit. Med. Bull.*, **2**, 207.
—— (1945) *Brit. Med. Bull.*, **3**, 96.
——, SHAW, D. P., and YOUNG, F. G. (1941) *J. Endocrinol.*, **2**, 475.
DENT, C. E., PITT-RIVERS, R., and VAUGHAN, J. (1945) Personal communication.
DU BOIS, E. F. (1936) Basal Metabolism in Health and Disease, 3rd ed. London.
EMERSON, K., and BINKLEY, O. F. (1946) *J. clin. Invest.*, **25**, 184.
GLYNN, L. E., HIMSWORTH, H. P., and NEUBERGER, A. (1945) *Biochem. J.*, **39**, 267.
GRAHAM, G., and POULTON, E. P. (1912-13) *Quart. J. Med.*, **6**, 82.
GYÖRGI, P., POLLING, E. C., and GOLDBLATT, H. (1941) *Proc. Soc. exp. Biol. N.Y.*, **47**, 41.
HARRIS, H. A., NEUBERGER, A., and SANGER, F. (1943) *Biochem. J.*, **37**, 508.
HIMSWORTH, H. P. (1945) *Proc. R. Soc. Med.*, **38**, 101.
——, and GLYNN, L. E. (1944) *Lancet* (i), 457.
JOSIAH MACY Jr. FOUNDATION REPORT (1942) Conference on Bone and Wound Healing, December 11-12, New York.
KEYS, A., TAYLOR, H. L., MICKELSEN, O., and HENSCHEL, A. (1946) *Science*, **103**, 669.
KOCHER, R. A. (1914) *Dtsch. Arch. Klin. Med.*, **115**, 82.
LEYTON, G. B. (1946) *Lancet* (ii), 73.
LUSK, G. (1917) Science of Nutrition, 3rd ed. Philadelphia.
McCOLLUM, E. V., ORENT-KEILES, E., and DAY, H. G. (1939) The Newer Knowledge of Nutrition, 5th ed. New York.
MACRAE, T. F., HENRY, K. M., and KON, S. K. (1943) *Biochem. J.*, **37**, 225.
MADDEN, S. C., and WHIPPLE, G. H. (1940) *Physiol. Rev.*, **20**, 194.
MAUN, M. E., CAHILL, W. M., and DAVIS, R. M. (1945) *Arch. Path. Lab. Med.*, **39**, 294.
MELNICK, D. (1943) *J. Amer. diet. Ass.*, **19**, 762.
MILLER, L. L., and WHIPPLE, G. H. (1942) *J. exp. Med.*, **76**, 421.
MITCHELL, H. H. (1942) *J. Amer. diet. Ass.*, **18**, 137.
MOXON, A. L., and RHIAN, M. (1943) *Physiol. Rev.*, **23**, 305.
MUWAZI, E. M. K., TROWELL, H. C., and HENNESSY, R. S. F. (1942) *East African med. J.*, **19**, 40.
PATEK, A. J., and POST, J. (1941) *J. clin. Invest.*, **20**, 481.
ROSE, W. C. (1938) *Physiol. Rev.*, **18**, 109.
——, HAINES, W. J., JOHNSON, J. E., and WARNER, D. T. (1943) *J. biol. Chem.*, **148**, 457.
RUSAKOW, A. V. (1943) *Amer. Rev. Soviet Med.*, **1**, 145.
SACHAR, L. A., HORVITZ, A., and ELMAN, R. (1942) *J. exp. Med.*, **75**, 453.
SCHOENHEIMER, R. (1942) The Dynamic State of Body Constituents, Cambridge, Mass.
TAYLOR, G. F., and CHHUTTANI, P. N. (1945) *Brit. med. J.*, (i), 800.
THORN, G. W., ARMSTRONG, S. H., and DAVENPORT, V. D. (1946) *J. clin. Invest.*, **25**, 304.
TROWELL, H. C. (1942) *Trans. R. Soc. trop. Med. Hyg.*, **36**, 151.
—— (1943) *Trans. R. Soc. trop. Med. Hyg.*, **37**, 19.
UPADHYAY, S. N. (1944) *Indian med. Gaz.*, **79**, 193.
WEICHSELBAUM, T. E. (1935) *Quart. J. exp. Physiol.*, **25**, 363.
WHIPPLE, G. H. (1942) *Amer. J. med. Sci.*, **203**, 477.
WILLIAMSON, W. B. (1944) *J. biol. Chem.*, **156**, 47.
WILLS, L. (1933-34) *Indian J. med. Res.*, **21**, 669.
——, and EVANS, B. D. F. (1938) *Lancet* (ii), 416.
——, and MEHTA, M. E. (1929-30) *Indian J. med. Res.*, **17**, 777.

Owing to space shortage, this article could not be published in its entirety. The section on Protein Metabolism in Relation to Liver Injury has therefore been omitted. This subject has already been dealt with in these *Proceedings* (*Proc. R. Soc. Med.*. 1945. 38, 101).

Section of Endocrinology

President—L. R. Broster, O.B.E., M.Ch.

[*October* 23, 1946]

DISCUSSION: OVERACTIVITY OF THE ADRENAL CORTEX

Mr. L. R. Broster: *Adreno-genital syndrome. The results of unilateral adrenalectomy.*—In considering these results I will adhere to Gardiner-Hill's original clinical classification of virilism, which is here supported by a series of 103 unilateral adrenalectomies.

Virilism	Group I	Prepubertal.
	Group II	Postpubertal.
	Group III	Postpubertal of the fat or Cushing's type.
	Group IV	Menopausal.

This condition is distinguished by the appearance of male secondary sex characters in the female, and the more marked this feature is, the greater the suppression of the feminine sex characters and function. It depends upon the age of onset and the degree of hyperplasia of the adrenal glands, consequently there is a wide range of variation in the clinical manifestations. These may be summarized as follows:

In the Female.

(*a*) *Male changes.*—(1) There is a shift towards the male figure involving skeletal structure, muscular development, and disposition of body fat. (2) The clitoris is enlarged. (3) The voice deepens and the larynx is enlarged. (4) Skin changes, involving growth of hair of the male type and distribution, occasionally baldness, coarsening of the texture of the skin with acne.

(*b*) *Female changes.*—(1) The breasts either do not grow, remain small, or may retrogress after full development. (2) The labia and vagina are poorly developed. (3) The uterus may be small and infantile. (4) The ovaries may remain immature, or later become cystic and degenerate. (5) The menses may never appear; if they do they become irregular, scanty or cease altogether. (6) Fertility is decreased.

(*c*) Associated with these somatic changes certain psychological symptoms may appear. These patients tend to react morbidly to their condition, they are depressed, frustrated and feel inferior beings socially. In some there are definite changes in sexuality and personality and in a few frank psychosis.

GROUP I.—15 CASES

Clinical.—Here the symptoms arise before or during puberty, when the secondary sex characters and feminine function fail to appear. Before puberty there may be an enlarged clitoris and a premature appearance of pubic hair. The figure resembles that of a boy more than a girl; and the chest is flat. I have operated on fifteen cases, varying in age from 5 to 31, with an average age of 16: three at the ages of 5, 6 and 7 with signs of precocity, and twelve, after the age of puberty. They all had male figures, hirsuties, deep voices, enlarged clitorides, either small or no breasts and primary amenorrhœa. Their sexuality is indefinite at this early age but in two over the age of 25 male and female tendencies alternated.

Pathology.—The weight of the adrenal glands removed in this series has ranged from 10 to 48 grammes, and there has been little to choose between the size of the two glands. The right adrenal was removed on five occasions, and the left on ten. The larger the gland the more pigmented it is, and resembles the spleen in colour. The cells are strongly fuchsinophil.

The results of estimations of 17-ketosteroid output in mg. per day are as follows:

Patient	Age		Pre-operative	Post-operative
HA	5		6	4
Ba	6		12·4	8·7
Eg	7		37	22
Mot	12		32	25·7
Sim	16		43	16·6
Her	17		54	27
Ron	22		75	58·7
		Average	37	23

It will be seen from these results that the 17-ketosteroid excretion rises with increasing age. The third patient Eg gives a good idea of the inexorable progress of this condition. She had an unusually high 17-ketosteroid output of 37 mg. at the age of 7 when I removed the left and larger of the two adrenal glands. During puberty the clinical condition became worse, and she became an embarrassing social problem to her family. She also had an elder brother with sexual precocity. At the age of 14, her 17-ketosteroid output had advanced to 100 mg. a day, a rise of 63 mg. in seven years, and I removed 19/29 grammes in weight of the remaining adrenal gland, with fatal results. Three patients who had been operated on before these biochemical tests were available showed an average 17-ketosteroid excretion of 60 mg. between two and five years after operation. There have also been two fatalities in this group after unilateral adrenalectomy, and all have passed into a state resembling acute hyperthyroidism, with a falling blood-pressure and a rising pulse-rate. We have found Lugol's solution extremely helpful in these advanced cases after operation but they constitute a major surgical problem.

From our experience so far it would seem that the limits of surgery begin to be reached when each gland weighs over 25 grammes and where the 17-ketosteroid output exceeds 100 mg. a day, but the other patients have done well and lead active and useful lives and, although the post-operative 17-ketosteroid output appears to rise with age, their clinical condition has not ostensibly worsened. The question is whether these results warrant adrenalectomy? The answer to this question is, how much more rapidly would the clinical condition deteriorate with both the adrenals intact. Surely the patient is entitled to whatever amelioration there is, even at considerable risk, for an otherwise desperate and hopeless condition. It is reasonable to argue that earlier operation may offer a better chance in preventing clinical deterioration which seems to become more accentuated during puberty. Consequently I have assessed the results of this group as *in statu quo*.

GROUP II.—88 CASES

This group includes 15 patients with definite psychological symptoms, 14 with the fat or Cushing's type—Group III—and one with the post-menopausal type. The patients, after passing normally through puberty, begin to develop hirsuties and menstrual irregularity, the periods tending to become scanty or to cease for months or even years. The hair is of male distribution and varies in amount and texture. Changes involving the body contour and the secondary sex characters are less prominent than in Group II.

Pathology.—The weight of the adrenal glands removed has varied from 2·3 to 8·8 grammes and the fuchsin reaction is generally present. We have found a definite correlation between the intensity of the stain and the physical condition.

Biochemical.—The biochemical tests have been performed by Dr. Patterson and Dr. Payne, and their results on 41 cases expressed as mg. 17-ketosteroids excreted per day are shown in the table:

	Pre	Post
Group II average 41 tests	17·6	8·5
good results	17·5	6·8
improved	19·1	9·9
i.s.q.	15·1	8·4

The average drop is roughly 50% and where this fall is greater, leaving the post-operative figure low, the results are better.

Clinical results.—The clinical results may be tabulated as follows:

Average age 26. Observed over 16 years. Mortality nil

	Cases	Cushing's	Psychological
Group II	88	14	15
Good	16	2	5
Improved	45	11	8
i.s.q.	10	1	2
Deficient information	14	—	—
Died from other causes	3	—	—

In this group there has been no operative mortality. Should the remaining adrenal hypertrophy or the 17-ketosteroid output increase there is no clinical evidence that they produce any marked deterioration. In suitable cases, therefore, it may be said that unilateral adrenalectomy is capable of arresting the progress of the disease.

Assessment of results.—The clinical results assessed in this table are my own and are based on the psychosomatic reaction of the patient to the operation, and on an evaluation of the alleviation of individual symptoms.

I therefore will proceed to quote observations from two independent sources, which accord in general with my own.

The first is the observations of my old house surgeon, Dr. Geoffrey Andrew, who carried out a postal follow-up, and the second is the record of a typical case by Dr. S. Leonard Simpson.

The report by Dr. Andrew:

(1) *Migrainous headache and depression*.—One or both of these symptoms were present in nearly every case. The headache was abolished in most cases; even where the operation had failed in other respects—e.g. in reducing hypertrichosis or obesity, it succeeded here. Many of the patients were thoroughly grateful for this relief. Some cases were still depressed at times after operation; this was usually because the hypertrichosis had not diminished as much as expected.

(2) *Hypertrichosis*.—Moustaches, beards or side whiskers were usually the main feature that drove the patients to seek advice in the first place. In most cases it produced noticeable psychological

reactions, unless these are to be considered as primary to the syndrome, i.e. part of the syndrome and not a result of it. Most of the patients were prepared to go to much trouble to get rid of the excessive hair.

The operation in some cases only produced good results. The operation only once or twice seemed really to have abolished the hairiness completely enough to allow the patient to call herself normal. In many more cases the adrenalectomy reduced the hirsuties sufficiently to allow of easy removal of the hair with tweezers. A few patients noticed the hair diminished both in abundance and coarseness, and were grateful enough for this. The majority of patients were satisfied with their own degree of improvement. The rest were frankly dissatisfied. This was either because they had observed no improvement, or because they had been led to expect excellent improvement probably by injudicious reports in the public press about it.

I might add that it is as difficult to persuade a woman to shave or remove her hair after operation as it is to dissuade her from operation when this is, as it sometimes is, the main symptom.

(3) *Obesity.*—As obesity was not a feature in all cases, these remarks apply to those where it was present, and the patients were worried by it. In some the operation produced excellent results. In others it was disappointing.

(4) *Periods.*—Many of the patients complained of irregular menstruation. Some had premenstrual dysmenorrhœa and had it severely. Most of the patients obtained some relief in this respect—either relief from dysmenorrhœa, or the occurrence of more regular periods. Some got little or no relief. There was a tendency among the patients to use the improvement in the periods as a yardstick of success of the operation. Those cases where conception occurred were very grateful, and this was one of the really encouraging features of the operation, as sterility was complained of in quite a few cases.

(5) *General health.*—This improved in nearly all cases. Even some of those cases labelled as "neurotic" confessed to me that they had been in better general health than hitherto.

Conclusions.—In well-selected cases the operation is undoubtedly successful in amelioration of the symptoms. In others it has failed. These were cases who pressed for the operation in spite of warning, and the correspondence made this clear.

I consider this is a clear and fair statement of the effects of operation on individual symptoms, and where it succeeds in some it may fail in others. There are obviously complex factors concerned in such a wide range of symptomatology, in which the adrenal plays an important and variable part in a polyglandular syndrome, and it is obvious that the present state of our knowledge does not enable us to predict with precision the amount of benefit that will take place in any given individual.

Dr. S. Leonard Simpson's case:—

A woman aged 26 years had married at the age of 17 and had had two miscarriages. She contracted gonorrhœa from her husband and was operated upon for pelvic peritonitis. She was subsequently divorced, and lost all interest in her sexuality.

For the past fourteen months she began to experience menstrual irregularity with diminishing flow from four to one day with bouts of amenorrhœa. During this time abnormal hair began to grow on her face, legs, and abdomen. She was worried, depressed and self-conscious about her condition and began to shun society.

In June 1944 her left adrenal was removed. It weighed 8 grammes. There were two subcortical adenomas. Vines's ponceau-fuchsin stain gave a moderately intense positive result in the zona fasciculata where the hypertrophy was most marked. The 17-ketosteroid excretion rose from 12·6 in 1943 to 17 and 19·3 mg. in 1944. After operation it dropped to 13·5. Dr. Simpson wrote in August 1946 "you will be very pleased with the result of the operation, and certainly there is positive evidence, both subjective and objective, of a degree of amelioration amounting to clinical cure. Since the operation the hair has completely fallen off the sides of the face and persists on the chin and upper lip in a very much finer texture than before operation. This is also true of her legs, on which, when she shaves them, no black spots are left as there were before operation. She plucks the hair off her face and bleaches the hair, but is certainly successful in her efforts, whereas before operation she could not control the growth of hair. All the hair round the nipples has disappeared; also the upgrowth of hair from the pubis to the umbilicus, which was previously *triangular in form,* but is now limited horizontally, as in the more normal female. My examination confirms the above, and in addition I noticed that the pubic and axillary hair was, if anything, somewhat scanty. The rather unusual feature is her report of loss of hair on the vertex of the head, receding from the temple, immediately after adrenalectomy. It then grew again, and fell out after influenza last winter. It grew again after this, but has now receded from the temples and is coming out in some degree generally. This is somewhat anomalous, as loss of hair of the head is usually associated with growth of hair on the face and body. The texture of the hair of the head is much finer, in contrast to its coarsening and thickening at the same time as the hair grew on her face. She also reported that her breasts had grown to normal size again, and that she had put on a little fat around her hips. She has not, however, gained appreciably in weight. On referring to my previous notes, I see she lost some weight with the onset of the disorder, and I then ascribed it to associated anxiety. However, it may well have been to loss of womanly fat, as occurred in Gordon Holmes' case. A cousin remarked at the onset of the trouble that she became as flat as a board, and lost her womanly shape, which she has now regained. As to menstruation she had almost complete amenorrhœa before the adrenalectomy, but after this there was a slight show (three days later) and ever since she menstruates regularly at intervals of twenty-six days, each menstruation lasting three days and being normal in amount. Her clitoris was enlarged before operation, and has in my opinion receded to normal size. Although restless and somewhat unstable, her general outlook has changed from deep depression and desperation to one of happiness and cheerful expectancy, amounting almost to euphoria. She is friendly with someone whom she anticipates might become her husband.

Psychological results.—Whatever the problem of cause and effect may be there is now sufficient evidence to say that definite improvement in psychological outlook can occur after operation in those patients where it was abnormal before. In fifteen cases there has been improvement in thirteen with failure in two. One of the latter was a German refugee, who had lost her relatives and spoke no English. She was operated upon during the war at a time when I was unable to obtain expert psychological help and guidance. The other lived at a distance and quarrelled with an elderly husband with stepchildren.

As this syndrome carries with it characters which are not normally feminine it is not surprising that these women resent what is fundamentally an unjust biological and social imposition. They become emotionally upset, shy, secretive, self-conscious, frigid and depressed to the point of desperation. Later they may become difficult to manage, wayward, capricious, unco-operative, slovenly in their appearance and habits, and may develop actual delusions of persecution and ostracism. It is not surprising that any amelioration of their physical and functional disabilities should be followed by an improvement in their general outlook. More obscure is their increased sexuality, the feeling of euphoria and sooner or later the loss of their delusional states which follows operation. The biochemical results in this group are too small to form any definite opinion, but the most successful have shown a comparatively low pre- and post-operative 17-ketosteroid output with a post-operative fall of over 50%.

Two of the most advanced cases in this series have been published by Clifford Allen and have remained well for eight and two years respectively.

Dr. E. F. Scowen and Dr. F. L. Warren: *Biochemical aspects of over-activity of the adrenal cortex.*—In 1931 Butenandt isolated androsterone, the first male hormone, from normal male urine. Three years later dehydroisoandrosterone was obtained from the same source. These pioneering researches have been followed in recent years by an intensive search in both normal and pathological urines for other steroid substances and the list of steroids now known to occur in urines from normal or diseased persons is a long and impressive one.

Four different 17-ketosteroids are now recognized as existing in the urine of normal men and women. Two of these are the pair originally isolated by Butenandt, namely, androsterone and dehydroisoandrosterone; the other two are stereoisomers of androsterone. Two of these substances are precipitable with digitonin (dehydroisoandrosterone and isoandrosterone) and are called beta-17-ketosteroids; the other two are not precipitable and are alpha-17-ketosteroids. Normally the alpha-17-ketosteroids account for 90% of the total 17-ketosteroids.

The studies of the Callows and of Hirschmann on urines from ovariectomized women and from eunuchs made it clear that the adrenals are chiefly responsible for the excretion of androgens. All later studies of urines from cases of adrenal hyperplasia or neoplasia have amply confirmed the adrenal cortical origin of the urinary 17-ketosteroids.

Proof of the adrenal origin of 17-ketosteroids led to the suggestion that quantitative estimation might be of value in diagnosis. Such estimation was impracticable so long as capon assay remained the only method for quantitative determinations. A careful study by the Callows of a colour reaction first discovered by Zimmermann led to a practical method for the chemical estimation of urinary 17-ketosteroids.

With the advent of a colorimetric method a wide survey of normal and pathological urines became possible and during the past eight years many thousands of specimens have been examined in laboratories in all parts of the world. We cannot do more than summarize the results under a few rather arbitrary headings.

Excretion of 17-ketosteroids in normal subjects.—It is not possible to classify a urine as male or female on the basis of its ketosteroid content. But the *average* 17-ketosteroid content of male urines is about 5 mg. per day higher than the *average* content of female urines. The earliest work tended to an average value of 8 mg./day for females and 13 mg./day for males. Recent determinations indicate that these values are probably too low and our own results give 13 mg./day for females and 18 mg./day for males. The difference of 5 mg./day may represent the testicular contribution.

Individual variation.—In both sexes the normal physiological range of excretion is very wide. In normal men we have found values from 9 mg. to 28 mg./day. In normal women the range is even wider since values of from 4 mg. to 23 mg./day, have been obtained in apparently normal individuals. It is impossible to stress too highly the importance of bearing in mind the wide physiological ranges of these excretions when interpreting cases suspected of abnormality.

Our experience of a large number of normal and abnormal urines has led us to the conclusion that the excretion in any individual is relatively constant. We have not encountered cases of rapidly fluctuating excretions. In practice this means that one determination of 17-ketosteroid output is usually sufficient to establish the *level* of excretion in an individual.

Our present knowledge of excretion in the normal subject is by no means complete. The available data tend to be crowded in the age-group 20 to 30 years. At both ends of the age-scale our knowledge is much more meagre. In children the excretion increases up to the age of puberty. Talbot quotes values of 1·3 mg./day in children of 4 to 7 years; 4·0 mg. at 7 to 12 years; and 8·2 mg. at 12 to 15 years. We are almost completely ignorant of the excretion in the newborn infant, although such data would frequently be of the highest value. Excretions in old age are still largely unexplored though recent advances in our knowledge of prostatic disease makes such information of great importance.

Levels of excretion in disease.—We may adopt a rough classification of hypofunction and hyperfunction.

Hypofunction: This includes Addison's disease and cases exhibiting pituitary anterior lobe deficiency. In Addison's disease the chief feature is destruction of adrenal cortical tissue and we accordingly find low levels of 17-ketosteroid excretion. Outputs from males tend to be higher than those from females and here again this excess may represent testicular contribution. In the later stages of the disease, however, values approaching zero are found in both sexes.

The effect of anterior pituitary deficiency is presumably caused primarily by absence of adrenocorticotrophic hormone. This is reflected in the extremely low outputs of 17-ketosteroids found in this condition. Administration of adrenocorticotrophin leads to increased output of 17-ketosteroids.

Hyperfunction: Two types may be considered. The first in which the defect is primarily in the adrenal. The second in which the abnormality is one of the anterior pituitary lobe.

In considering non-neoplastic cortical abnormalities we include pseudohermaphroditism in the newborn, and the adreno-genital syndrome, both pre- and post-puberal, in the female.

Interpretation of results on newborn pseudohermaphrodites is impossible at the moment owing to lack of data on normal excretion.

Excretions of 17-ketosteroids in prepuberal virilism caused by benign hyperplasia of the cortex may be extremely high—more than 100 mg./day. Such high values are also associated with cortical carcinoma. But qualitative examination of the steroids from proved cases of benign hyperplasia has shown that, with few exceptions, androsterone is the component that is augmented and that it is this substance that is chiefly responsible for the high total output.

The effect of excision of a hyperplastic adrenal has been, in our experience, by no means regular. In some cases an already high excretion, present before operation, has been increased post-operatively. A possible explanation is that removal of cortical tissue also removes its restraining influence on the secretion of adrenocorticotrophic hormone and this is followed by overcompensated hypertrophy and secretion by the surviving adrenal gland.

Virilism in the adult woman usually results in excretions at or above the upper normal range. Values up to 40 mg./day are regularly encountered. Unlike the prepuberal cases, adult virilism does not lead to the very high outputs of more than 100 mg./day.

Adrenal cortical carcinoma.—Carcinoma of the adrenal cortex in females of all ages is almost always associated with high excretions of 17-ketosteroids. A few exceptional cases have been reported in which the output has not exceeded normal limits. A common factor is the greatly increased excretion of dehydroisoandrosterone and all later work has confirmed the original suggestion of Crooke and Callow that excessive amounts of this steroid are characteristic of carcinoma.

The rarity of adrenal carcinoma in males has limited the opportunities for investigation. In 1936 one of us isolated an unusual 17-ketosteroid from such a case. This substance was considered to be an artefact and the problem arose as to whether its precursor was dehydroisoandrosterone or some other steroid. This problem is still unsolved. There are objections to the assumption that dehydroisoandrosterone is the precursor and it still appears possible that cortical carcinoma in the male does not resemble this tumour in the female in its sterol metabolism.

Hyperfunction of the anterior pituitary.—In this group we may include basophilic and acidophilic hyperplasia or neoplasia.

In Cushing's syndrome excretions of up to 40 mg./day are common. Extremely high outputs are not found.

In the acromegalic, a study of individual cases gave interesting results. Such cases frequently show normal or slightly elevated excretions. But occasionally very high outputs can be detected. In two cases, for example, a male excreted 110 mg./day and a female 70 mg. The excess of androgen in each case was shown to be androsterone. Preliminary results appear to show that the level of excretion is related to the phase of activity of the disease.

As a summary of this brief review of 17-ketosteroid estimations during the past eight years we might repeat what Callow wrote at the beginning of that period, namely: "The independent diagnostic value of urinary 17-ketosteroid excretion is limited to cases of adrenal cortical tumour; in conjunction with other evidence they have confirmatory value in cases in which lowered adrenal cortical function is suspected."

Brief mention may be made of another approach to the study of adrenal cortical function. It has been shown that human urine contains substances resembling in chemical characteristics and biological action certain of the 11-oxycorticosteroids. Urinary extracts have been prepared which are effective in maintaining life in adrenalectomized animals, in protecting such animals against exposure to cold, in preventing water intoxication, and in depositing glycogen in the liver of the adrenalectomized animal. No active compounds have yet been isolated from urine but since the extracts are active with respect to carbohydrate metabolism it is assumed that at least one active compound bears an oxygen atom in the 11-position.

Biological assays show that these substances are excreted in increased amounts by post-operative, burned, or otherwise damaged persons. These findings appear to substantiate the view that the adrenal cortex plays a part in the reaction of the organism to such stresses.

Recently it has been shown that these "cortin-like" substances in human urine may be satisfactorily estimated by chemical methods. By virtue of their side chains all active corticosteroids have reducing properties and they can be estimated by micro-reduction methods. Correlation between chemical and biological assays is good.

Although these researches are still in the exploratory stage some interesting results have already come to light. The normal output of corticosteroids in adults of both sexes is about the same and amounts to about 0·25 mg./day. The physiological variation is wide, since normal excretions of 0·1 to 0·4 mg./day are found. Of conditions so far investigated that lead to increased excretions of "cortin-like" substances, Cushing's syndrome is outstanding. In one patient an output of 12 mg./day was observed, that is, about fifty times the normal excretion. This may be exceptional but two of our own cases showed excretions of 5 and 6 mg./day, and all have been high.

The chemical estimation is non-specific and the possibility existed that the active material might form but a small fraction of the total estimated chemically. However, it appears from some results that we have recently obtained that the chemical method does give substantially a true figure for corticosteroid content of urinary extracts. Corticosteroids can be estimated polarographically by virtue of the characteristic unsaturated ketone grouping situated at the end of the molecule opposite to the grouping involved with reduction. Parallel experiments have shown that at least 50 to 60% of the material determined chemically is active polarographically and hence carries the characteristic corticosteroid group.

Adrenal cortical hyperplasia does not appear to increase the corticosteroid excretion but does increase 17-ketosteroid output. On the other hand, in Cushing's syndrome, the corticosteroid output is very greatly augmented while the 17-ketosteroid excretion is but little elevated. It appears possible, in fact, that the corticosteroid production and the 17-ketosteroid production (or at least production of 17-ketosteroid precursors) are not necessarily linked. Furthermore, it is possible that there are two distinct adrenocorticotrophic hormones elaborated by the anterior pituitary one of which stimulates corticosteroid production and the other androgen production in the adrenal cortex. The androgenic stimulation that can occur in acromegaly and the increased corticosteroid production in basophilism are very interesting in this connexion.

(NOTE.—In quoting actual figures for steroid excretions we have drawn mainly on our own data, that is, on results obtained either at The Chester Beatty Research Institute of the Royal Cancer Hospital (Free), or by Mrs. A. M. Robinson, at St. Bartholomew's Hospital. In discussing the 17-ketosteroid levels of normal urines we have made free use of results recently obtained in joint work with Dr. Morris and Dr. Barnett of the Endocrine Unit of the London Hospital. We should also like to thank all those clinical friends who have placed their material so freely at our disposal.)

Dr. A. C. Crooke: *The altered physiological activity in hyperfunction of the adrenal cortex.*—The endocrine symptoms associated with hyperplasia and tumours of the adrenal cortex are variable. In the adult female the clinical picture of virilism is the most common and it has been dealt with by Mr. Broster. The other well-known clinical picture is that of basophilism but there also exists a number of confusing intermediate types between virilism and basophilism. The final criterion of basophilism is the finding of hyaline basophil cells in the anterior lobe of the pituitary gland which I described in 1935. These cells are found in the pituitary glands of all patients with basophilism whether there is no tumour in any of the endocrine glands, a chromophobe or a basophil adenoma in the pituitary gland, or a tumour of the adrenal cortex, thymus or ovary. Hyaline basophil cells do not occur in the pituitary glands of patients with virilism alone. Thompson and Eisenhardt (1943), writing from the Brain Tumour Registry at Yale, confirmed my findings in a large series of pituitary glands from patients with all forms of basophilism but they could not find hyaline basophil cells in the pituitary glands of any of their patients with virilism, nor in borderline cases in which virilism was associated with glycosuria or hypertension and they did not accept the latter as cases of basophilism on this account. Obviously considerably more pathological material will have to be collected from these intermediate types in order to elucidate this matter.

The reason why some patients with adrenal cortical hyperplasia or tumours develop virilism and others basophilism is not known. Interesting theories about the causation of basophilism have been put forward by Albright (1942) and by Kepler (1945), both of whom regard all forms of basophilism as due to "hyperadrenocorticism," and they consider that the changes in the pituitary gland are secondary to this. My contention that the hyaline change does not constitute a degenerative condition of the pituitary basophil cells has been upheld on cytological grounds by Rasmüssen (1936), McLetchie (1944), and Mellgren (1945). I cannot agree that the pituitary change is necessarily secondary to adrenal cortical hyperfunction but it is probably true that virilism and basophilism are associated with the production of an excess of different types of steroid substances derived from different types of cells in the adrenal cortex. Grollman (1936) has suggested that the androgen secreting cells are derived from a special "androgenic zone" supposed to exist in the innermost layers of the cortex adjacent to the medulla and his theory has been widely accepted. Zwemer, Wooton and Norkus (1938) have shown, however, that the adrenal cortex grows continuously from cells just beneath the capsule which differentiate progressively into the cells of the zona glomerulosa, fasciculata and reticularis and that finally they degenerate in the innermost layer adjacent to the medulla. This is confirmed by our own findings that after hypophysectomy the adrenal cortex atrophies progressively from within outwards and no definite histological abnormality occurs in the outermost zone (Crooke and Gilmour, 1938). If this is true, it is unlikely that a layer of special androgen-secreting cells exists in the region adjacent to the medulla. Cahill, Melicow and Darby (1942) found that adrenal cortical tumours unassociated with abnormal hormone activity were composed of cells which were almost devoid of lipoid vacuoles, while in those which were associated with virilism only there were many vacuoles, and those associated with Cushing's syndrome were choked with vacuoles forming large "foam cells". All these cell types may be found in the normal adrenal cortex and according to Zwemer represent different stages in the elaboration and secretion of its hormones.

It is generally believed that the androgenic steroids are breakdown products chiefly of adrenal cortical but also of certain other steroid hormones. I consider that in hyperplasia and tumours of the cortex associated with virilism they are probably derived from incompletely elaborated hormones. These would be produced by intermediate cells which have not yet developed into ripe secreting cells. The excessive production of the vital adrenal cortical steroids like desoxycorticosterone from fully developed or ripe cortical cells in patients with basophilism would, however, be stimulated by the excessive production of adrenotrophic hormone, evidenced by the hyaline change in the basophil cells of the pituitary glands. This would explain several perplexing observations. It would account for the very high androgen output in patients with virilism caused by adrenal cortical tumours composed of incompletely developed cells and the lower output in patients with basophilism caused by tumours composed of completely developed or ripe cells which produce vital adrenal cortical hormones (Cahill, Mellicow and Darby). Secondly, it would account for the remarkable unilateral atrophy of the adrenal cortex in patients with basophilism associated with a tumour of the other adrenal. Such tumours produce a great excess of vital cortical steroids and it has been shown that certain vital steroids cause cortical atrophy in the experimental animal. Conversely in women with virilism caused by an adrenal cortical tumour the opposite adrenal is not atrophied as would be expected if only incompletely elaborated hormones are being produced. Thirdly, it would explain the occasional incidence of Addison's disease in children with adrenal cortical hyperplasia often associated with pseudohermaphroditism or pubertas præcox without basophilism (Di Ruggiero and Jolly, 1938; Dijkhuizen and Behr, 1940; Butler, Ross and Talbot, 1939; Wilkins, Fleischmann and Howard, 1940; Thelander and Cholffin, 1941). In these patients large amounts of androgens are produced to the exclusion of vital hormones. Finally it would account for the normal or only slightly increased output of androgenic steroids in patients with basophilism without adrenal cortical tumours. In this condition the anterior pituitary gland acting as the instigator stimulates both adrenal cortices and this results in bilateral cortical hyperplasia and the production mainly of completely elaborated vital steroids.

To summarize then, hyperfunction of the adrenal cortex is a difficult and controversial subject. Two main types of hyperfunction are encountered. I have suggested as a working hypothesis that the first, which is associated with the clinical picture of virilism, is caused by an over-production of androgenic substances derived from incompletely developed adrenal cortical cells and associated with no excess of anterior pituitary secretion. The second, which is associated with the clinical picture of basophilism, is caused by an over-production of the fully elaborated or vital adrenal cortical hormones derived from completely developed or ripe adrenal cortical cells and stimulated by an excess of anterior pituitary secretion, which is, in effect, the driving force responsible for this complete development of cells and complete elaboration of hormones in basophilism.

BIBLIOGRAPHY

ALBRIGHT, F. (1942) Cushing's Syndrome. The Harvey Lectures, 38, 123.
BUTLER, A. M., ROSS, R. A., and TALBOT, N. B. (1939) *J. Pediat.*, 15, 831.
CAHILL, G. F., MELLICOW, M. M., and DARBY, H. H. (1942) *Surg. Gynec. Obstet.*, 74, 281.
CROOKE, A. C. (1935) *J. Path. Bact.*, 41, 339.
——, and GILMOUR, J. R. (1938) *J. Path. Bact.*, 47, 525.
DIJKHUIZEN, R. K., and BEHR, E. (1940) *Acta Pædiat.*, 27, 279.
DI RUGGIERO, and JOLLY, A. (1938) *Ann. d'anat. path.*, 15, 332.
GROLLMAN, A. (1936) The Adrenals. London.
KEPLER, E. J. (1945) *J. Clin. Endocrinol.*, 5, 70.
MCLETCHIE, N. G. B. (1944) *J. Endocrinol.*, 3, 332.
MELLGREN, J. (1945) *Acta. Path. Microbiol. Scandinav.* Supplement 60.
RASMUSSEN, A. T. (1936) *Endocrinol.*, 20, 673.
THELANDER, H. E., and CHOLFFIN, M. (1941) *J. Pediat.*, 18, 779.
THOMPSON, K. W., and EISENHARDT, L. (1943) *J. Clin. Endocrinol.*, 3, 445.
WILKINS, L., FLEISCHMANN, W., and HOWARD, E. J. (1940) *Endocrinol.*, 26, 385.
ZWEMER, R. L., WOOTON, R. M., and NORKUS, M. G. (1938) *Anat. Rec.*, 72, 249.

Dr. A. S. Parkes: It is clear from the remarks of previous speakers that estimation of the urinary 17-ketosteroids is now widely used to assist the differential diagnosis of various forms of adrenal over-activity, and that such an estimation may be a useful test. On the other hand, one must be careful to recognize the limitations of the technique. The emphasis on the 17-keto components of the steroid complex arose originally not from any conviction as to their special importance, except in the case of extensive neoplastic growth of the adrenal cortex, but from the fact that they could be estimated fairly easily by non-biological methods. It would be most unfortunate if concentration on the 17-ketosteroids retarded the investigation of other groups of substances and other methods of differential diagnosis.

Dr. S. L. Simpson: I am glad to be able to confirm the excellent result of unilateral adrenalectomy in the case to which Mr. Broster referred; but I may say that I regard the result as exceptionally good, I have seen several patients suffering from the adrenogenital syndrome, who, having undergone unilateral adrenalectomy by Mr. Broster or other skilful surgeons, failed to secure appreciable benefit as regards hirsutism or adipose deposition, although they belonged to the relatively favourable Group II. It is, however, not uncommon for amenorrhœa to be favourably influenced. A long interval between puberty and virilism and a progressive rise in urinary androgens are relatively favourable prognostications.

In one virilized woman of 22, under my care, removal of a large right adrenal adenocarcinoma by Mr. W. M. Dickson in 1938 led to regular menstruation after previous amenorrhœa, but no effect whatsoever on a severe generalized hirsutism. The urinary 17-ketosteroids fell from a pre-operative 143 mg. per twenty-four hours to 25 mg., and after two months rose again to 62 mg. at which approximate level it has remained for six years.

In December 1933 I demonstrated, at the Clinical Section of this Society, a woman with an adrenogenital syndrome in whose urine de Fremery and I had demonstrated, for the first time, a gross excess of comb-growth (capons) and prostate stimulating (castrated rats) hormone. The subsequent development of the work (1936) has opened up wide fields. The 17-ketosteroid assay is a useful blunderbuss method, but concomitant biological assays should not be omitted in research.

they degenerate in the innermost layer adjacent to the medulla. This is confirmed by our own findings that after hypophysectomy the adrenal cortex atrophies progressively from within outwards and no definite histological abnormality occurs in the outermost zone (Crooke and Gilmour, 1938). If this is true, it is unlikely that a layer of special androgen-secreting cells exists in the region adjacent to the medulla. Cahill, Melicow and Darby (1942) found that adrenal cortical tumours unassociated with abnormal hormone activity were composed of cells which were almost devoid of lipoid vacuoles, while in those which were associated with virilism only there were many vacuoles, and those associated with Cushing's syndrome were choked with vacuoles forming large "foam cells". All these cell types may be found in the normal adrenal cortex and according to Zwemer represent different stages in the elaboration and secretion of its hormones.

It is generally believed that the androgenic steroids are breakdown products chiefly of adrenal cortical but also of certain other steroid hormones. I consider that in hyperplasia and tumours of the cortex associated with virilism they are probably derived from incompletely elaborated hormones. These would be produced by intermediate cells which have not yet developed into ripe secreting cells. The excessive production of the vital adrenal cortical steroids like desoxycorticosterone from fully developed or ripe cortical cells in patients with basophilism would, however, be stimulated by the excessive production of adrenotrophic hormone, evidenced by the hyaline change in the basophil cells of the pituitary glands. This would explain several perplexing observations. It would account for the very high androgen output in patients with virilism caused by adrenal cortical tumours composed of incompletely developed cells and the lower output in patients with basophilism caused by tumours composed of completely developed or ripe cells which produce vital adrenal cortical hormones (Cahill, Mellicow and Darby). Secondly, it would account for the remarkable unilateral atrophy of the adrenal cortex in patients with basophilism associated with a tumour of the other adrenal. Such tumours produce a great excess of vital cortical steroids and it has been shown that certain vital steroids cause cortical atrophy in the experimental animal. Conversely in women with virilism caused by an adrenal cortical tumour the opposite adrenal is not atrophied as would be expected if only incompletely elaborated hormones are being produced. Thirdly, it would explain the occasional incidence of Addison's disease in children with adrenal cortical hyperplasia often associated with pseudohermaphroditism or pubertas præcox without basophilism (Di Ruggiero and Jolly, 1938; Dijkhuizen and Behr, 1940; Butler, Ross and Talbot, 1939; Wilkins, Fleischmann and Howard, 1940; Thelander and Cholffin, 1941). In these patients large amounts of androgens are produced to the exclusion of vital hormones. Finally it would account for the normal or only slightly increased output of androgenic steroids in patients with basophilism without adrenal cortical tumours. In this condition the anterior pituitary gland acting as the instigator stimulates both adrenal cortices and this results in bilateral cortical hyperplasia and the production mainly of completely elaborated vital steroids.

To summarize then, hyperfunction of the adrenal cortex is a difficult and controversial subject. Two main types of hyperfunction are encountered. I have suggested as a working hypothesis that the first, which is associated with the clinical picture of virilism, is caused by an over-production of androgenic substances derived from incompletely developed adrenal cortical cells and associated with no excess of anterior pituitary secretion. The second, which is associated with the clinical picture of basophilism, is caused by an over-production of the fully elaborated or vital adrenal cortical hormones derived from completely developed or ripe adrenal cortical cells and stimulated by an excess of anterior pituitary secretion, which

Clinical Section

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[*October* 11, 1946]

Bone Deformity Associated with Multiple Neurofibromatosis.—NORMAN C. TANNER, F.R.C.S.

The patient, aged 36, complained of a lump on the right leg which had been first noticed at the age of 4. Three years later the lump was diagnosed at a London hospital as congenital syphilitic osteoperiostitis and treated with iodides and leg irons. There is no record of a Wassermann reaction at this time. She was admitted to the same hospital when aged 20, because of a temporary sudden painful increase of the swelling. The Wassermann reaction was then negative.

The patient came to St. James' Hospital in 1941 and was delivered of a male child. It was noticed that she suffered from multiple neurofibromatosis, and her blood Wassermann reaction and Kahn test were negative.

A second child was born in 1944, and after this the leg tumour seemed to become even larger.

Family history.—The patient knows of no other member of her family with neurofibromatosis though both her children have the disease.

Clinical examination.—On examination early in 1946, the patient appeared to be well-nourished and intelligent, with no abnormality of heart, lungs or central nervous system. There were multiple coffee-coloured areas on all parts of the skin, and also numerous sessile and pedunculated nodules typical of von Recklinghausen's disease. The spine was definitely scoliotic, though this was not marked enough to produce any disability.

The left leg appeared normal but the right one had a large rather lobulated mobile subcutaneous tumour on the anterior, medial and to a lesser extent lateral surface of the right leg between patella and ankle-joint (*see* fig. 1).

There was lengthening of the right tibia (right tibia 17¼ in., left tibia 15½ in.) The fibulæ were of equal length, so that the normal relation of internal and external malleolus of the right leg was changed, the two being at the same level.

Many problems still await adequate answers:

(1) Adrenogenital syndrome. With amenorrhœa and hirsutism, the third feature of the syndrome may be either (*a*) developing adiposity or (*b*) loss of fat and muscular development. In either case removal of an adrenal cortex tumour will abolish the abnormality (*a*) or (*b*). Histologically the tumours are identical.

(2) Apparently identical adrenal cortex tumours in:
  (*a*) Women—result in virilism and a high secretion of androgens.
  (*b*) Men—feminization, impotence, and a high secretion of œstrogens.
  (*c*) Boys—pseudo-sexual precocity and a high secretion of androgens.

(3) An adrenal tumour in girls usually produces pseudo-sexual precocity with menstruation at the age of 8 or so, and a general hirsutism of face and body. However, Walter and Kepler recorded a case of menstruation at 19 months, pubic hair, but no body or facial hirsutism, and apparently cured by removal of an adrenal tumour at 5 years of age.

(4) Gross moustache and beard occur in many female members of one family with normal menstruation and normal body-weight. Such women show no other endocrine stigmata and bear children. There, hirsutism is genetically determined.

(5) In the adrenogenital syndrome due to adrenal tumour or hyperplasia, clinical diabetes is exceptional, although the tolerance curve shows a decreased carbohydrate tolerance. Sprague has recently described a woman of 49 with severe clinical diabetes who was cured by removal of an adrenal cortex tumour, but who had no endocrine stigmata.

REFERENCES

SIMPSON, S. L. (1934) *Proc. R. Soc. Med.*, 27, 383.

——, DE FREMERY, P., and MACBETH, A. (1936) *Endocrinol.*, 20, 363.

SPRAGUE, R. G., PRIESTLEY, J. J., and DOCKERTY, M. C. (1943) *J. Clin. Endocrinol.*, 3, 28.

WALTER, W., and KEPLER, E. J. (1938) *Ann. Surg.*, 107, 881.

Dr. J. Patterson: Dr. Warren's figures for 17-ketosteroid excretion of normal adults ranged higher than the usually accepted values, higher than my own findings, and also exceeded the recent values obtained by the more specific polarographic method. His reference to raised output after unilateral adrenalectomy conflicted with my own experience in which post-operative figures had always been the lower. The work of Mason and Kepler seemed to challenge the validity of accepting the excessive excretion of dehydroisoandrosterone as diagnostic of adrenal tumour in female subjects. It was given by only 5 out of 6 of their adrenal tumour cases.

Dr. R. K. Callow: Urinary hormone assays are indirect; the materials detected are metabolites of compounds active in the body. Biological assays do not detect inactive compounds derived from active androgens. Estimations of 17-ketosteroids detect the group present in certain androgens and known to survive metabolic change. While defending chemical methods I should like to emphasize again that the wide range of normal variation of 17-ketosteroid excretion is such that attempts to diagnose minor endocrine disturbances from minor variations are unlikely to be fruitful. Specific chemical diagnosis may be possible by isolation of compounds characteristic of gonadal or adrenal pathological activity, but is difficult and laborious.

shortening, lengthening, cysts of bone, or a tendency to spontaneous fracture have all been described.

Brooks and Lehman (*Surg. Gynec. Obstet.*, 1924, 38, 587), who record the osseous lesion in 7 cases, believe that it results from neurofibromatosis of the periosteal nerves. The growing tumour in the periosteum causes varying degrees of rarefaction and softening of the bone, which later may change to a stage of regenerative osteogenic activity. A thin layer of new bone may even be formed around the tumour producing an X-ray appearance like a bone cyst. Such "bone cysts" on removal are found to have a centre typical of neurofibroma. The lesion appears to share with acute infections the power of stimulating bone growth when situated near the metaphysis, or it may damage the metaphysis and lead to incomplete growth of the bone.

The case shown seems to be one where the tumour originated in the periosteum and some bone lengthening has been caused. It is probable that at an early stage of bone rarefaction and softening, the bone bent, and that this has been followed by regeneration and compensatory hypertrophy.

Ligation of the Inferior Vena Cava for Femoral Thrombosis with Pulmonary Infarction.—J. D. FERGUSSON, M.D., F.R.C.S.

H. J., male, aged 63, was admitted to the Central Middlesex County Hospital on February 4, 1946, suffering from thrombo-phlebitis of the right femoral vein and a recent left pulmonary infarct. Three weeks previously he had had influenza followed by thrombo-phlebitis in the right calf four days later. On the day before his admission to hospital he had experienced pain in the left side of his chest, become dyspnœic and coughed up blood-stained sputum.

On examination.—T. 102° F. Thrombo-phlebitis affecting the right femoral vein and clinical evidence of left pulmonary infarction. Subsequent treatment with sulphathiazole and penicillin brought about some improvement in the inflammatory condition, but on February 27 his sputum was again tinged with blood. After discontinuing penicillin on March 5 he developed thrombo-phlebitis of the opposite femoral vein which in turn was succeeded by evidence of a further pulmonary infarct. In order to minimize the risk of a lethal embolus the inferior vena cava was ligated at the level of the fourth lumbar vertebra. Post-operative heparinization and treatment with dicoumarin were employed, and recovery was uneventful.

No untoward changes occurred as the result of the operation, and the œdema of the legs, already present in association with the thrombo-phlebitis, did not increase. The œdema has now (six months later) subsided considerably, and he is able to walk several miles without undue fatigue. There has been some visible dilatation of the superficial collateral veins in the front of the abdomen, but this, though doubtless partly obscured by his obesity, has been considerably less than anticipated. It appears in general that inferior vena caval ligation is well tolerated, free from objectionable sequelæ, and is worthy of more universal consideration as a prophylactic against pulmonary embolism in cases exhibiting bilateral femoral thrombo-phlebitis.

Von Recklinghausen's Disease.—A. DICKSON WRIGHT, M.S., F.R.C.S.

Little girl, aged 7. Born with a large pigmented mole on the whole of the right half of the chest. Since birth other small lesions, nodules and *café au lait* patches, have developed elsewhere in the body. Recently a diffuse nodular and markedly tender tumour has developed in the left pectoral and axillary region with

X-ray shows the lengthening of the tibia. There is also anterior and medial bowing (fig. 2). There is great thickening of the cortex, maximal at the middle, but evident in the whole length of the bone except its highest and lowest few inches. The medulla is narrowed and there is an area of rarefaction in the upper tibia.

The right fibula has medial bowing and sclerosis of cortex, but the changes are much less than those in the tibia.

Operation.—On May 2, 1946, under general anæsthesia, the tumour was exposed through a long anteromedial incision. The tumour was encapsulated except on the tibial and fibular aspects, where it blended with the periosteum. The tumour was in two main masses, one weighing 1 lb. 10½ oz., the other 6 oz. An area of skin 25 cm. by 10 cm. was also removed to prevent redundancy.

Histological examination.—A neurofibromatous mass in the subcutaneous tissue, showing the unusual feature of a marked hyperplasia of nerve fibres. Also myxomatous change in several areas of the fibromatous part.

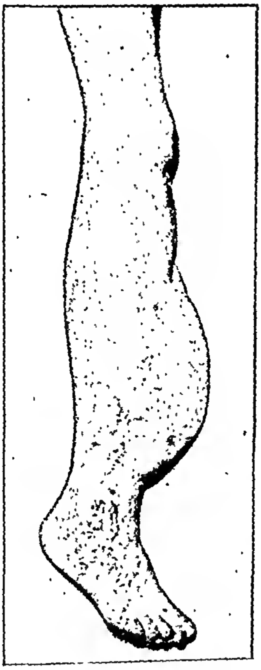


FIG. 1.

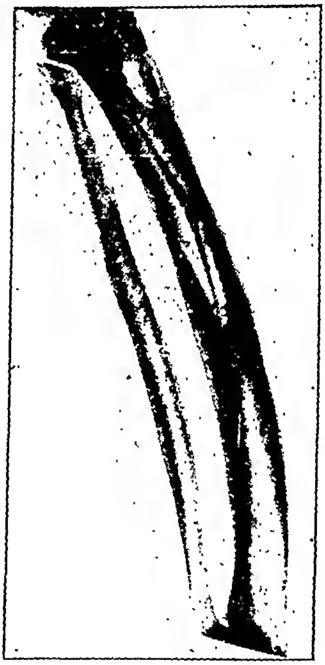


FIG. 2.

FIG. 1.—Side view of tumour before operation.

FIG. 2.—X-ray photograph showing bowing, lengthening, sclerosis and localized rarefaction. (*Photographs* by J. E. Andrews.)

Clinical result.—With the removal of the tumour masses, the underlying bony deformity has become very evident as the tibia can be palpated. The patient has gained complete comfort and is satisfied with the result, so no further cosmetic procedure is contemplated.

Discussion.—The commonest bony lesion described in this disease is scoliosis, and it probably results either from lesions in the intervertebral foramina or from inequality in the length of the legs as in this case. Rarefaction, hypertrophy,

Section of Medicine

President—Maurice Davidson, M.D.

[*November* 26, 1946.]

DISCUSSION ON BIRTH CONTROL: SOME MEDICAL AND LEGAL ASPECTS

Dr. Maurice Davidson (The President): Although the title of the Discussion may seem to imply a discussion restricted to certain specific and rather technical matters relation to conception and pregnancy, I hope very much that it will, on the contrary, be dealt with from a much wider standpoint, for indeed it embraces many aspects of human life and conduct, upon which the medical profession, and especially those in general practice, are liable to be consulted, and on which they are not unreasonably expected to be in a position to offer reliable counsel.

Now the ability to do this service to all who require it calls for a wide and sympathetic understanding of human problems as a whole. It needs, moreover, some acquaintance at least with various general principles which must underlie our whole conception of the meaning, the significance, and the objects of birth control, if our advice to our patients is to be of any real value.

It is important that the doctor should realize in what circumstances and for what reasons birth control may be necessary; whether the object of the control is merely to limit the procreation of children, or to preclude it altogether; whether such restriction in any given case is so urgent that if the woman is found to be pregnant, artificial termination of her pregnancy becomes an imperative measure; what are the present accepted indications for the induction of therapeutic abortion. and where is the dividing line between justifiable therapeutic abortion, and criminal abortion, of which, as you know, the law, as it stands at present, takes an extremely serious view. It is important that we should clearly understand just what the law is on this matter. It is also perfectly reasonable for us to debate, if we are so disposed, the question whether any alteration of the existing law is or is not desirable, and, if we feel that it is, then what steps we as medical men should take in a proper and constitutional manner in the endeavour to foster such alteration.

I would appeal to all who take part in this discussion to do their utmost to keep it on the broad basis which I have endeavoured to indicate.

Dr. E. B. Ford (Reader in Genetics in the University of Oxford): *The genetic aspects of birth control.*—It may in certain instances be desirable to advise birth control to patients suffering from hereditary disease and even to their normal relations. In these circumstances, birth control is, of course, directed not to a mere limitation or spacing of births but to ensuring that the individuals in question should beget no offspring. It might be thought that such advice could be given either owing to the possibility of direct and seriously harmful effects upon children or immediate descendants were such to be born, or for a more general eugenic reason: that of spreading dangerous hereditary disease through the population. Yet it will be shown that the latter consideration can rarely of itself be justified as a reason for recommending birth control.

Whether or not patients (or their near relations) suffering from familial disorders can properly be advised to resort to birth control depends upon the way in which such disease is inherited. If it be a simple *heterozygous* defect (often, and usually wrongly, called "dominant" in the literature) none but the affected can transmit the condition, but each sufferer will pass it on to half his or her children. When the disease is serious, this would appear to be reasonable grounds for considering the use of birth control. Moreover, in certain instances, affections so inherited do not manifest themselves until most of the family are born (e.g. Huntington's chorea, which rarely appears before the age of 30). Here even those children who are in reality normal may live under the shadow of becoming ultimately insane, and the fear of transmitting such an affliction to their sons and daughters.

On the other hand, those who suffer from *recessive* familial defects nearly always have normal parents. Their children too will be normal, but all of them will be heterozygotes, transmitting the hereditary condition. Not until two such heterozygotes marry will the disease reappear, and it will do so in one-quarter of the offspring of such a union. In respect of any recessive disease, the population is divided into three classes: those truly normal, those apparently normal yet transmitting the defect (the heterozygotes), and the actual sufferers (the recessives). These three types are disdistributed in the ratio $p^2 : 2pq : q^2$ in the population as a whole. Thus if only one person in 10,000 suffers from a given recessive defect, over 2% of the normal population are transmitting it. Clearly, then, hereditary units, or *genes*, are widely scattered throughout the population even when they are responsible for hereditary defects so rare as to be medical curiosities.

No eugenic measures are of the slightest avail to combat such a situation. Indeed it must be remembered that rare heterozygous, as well as recessive, defects are maintained in the population in equilibrium, balanced by selection tending to eliminate them and mutation tending to increase their frequency. Were it possible to prevent all those suffering from a given recessive disease from a change in the appearance of the overlying mammary gland resembling a precocious development of the organ (fig. 1).

At operation a large racemose tumour with extensive connexions in the axilla was removed; the mammary enlargement was due to an overgrowth of connective tissue such as is often found in the vicinity of the plexiform neuromata of von Recklinghausen's disease.

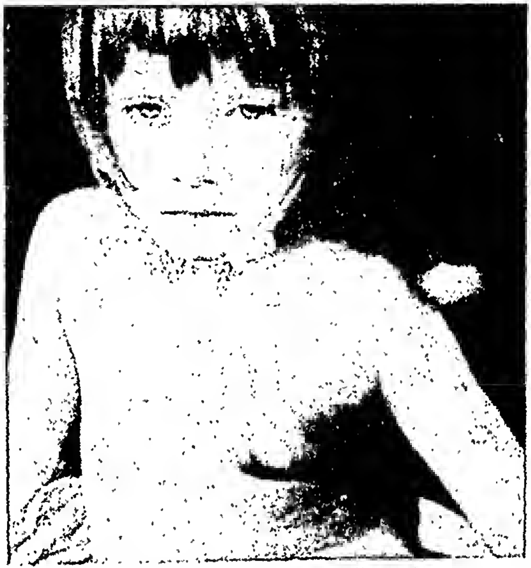


FIG. 1.—Von Recklinghausen's disease with unilateral mammary hypertrophy.

Total Gastrectomy with Œsophagoduodenal Anastomosis.—A. DICKSON WRIGHT M.S., F.R.C.S.

This patient, aged 63, complained of dyspeptic symptoms of a vague kind for one year and radiographic examination showed an extensive filling defect of the greater curvature.

The extent of the growth made a total gastrectomy necessary to get sufficiently wide of the growth. The case is shown to illustrate the method of uniting the duodenum to the œsophagus which is my normal practice. After freeing of the œsophagus from its hiatus in the diaphragm and dividing any fine bands on the outer side of the duodenal curve, there is no difficulty in suturing and no tension after completion, and no special stay sutures to the diaphragm are required. The suturing is done with two layers of fine deknatil interrupted sutures (fig. 1).

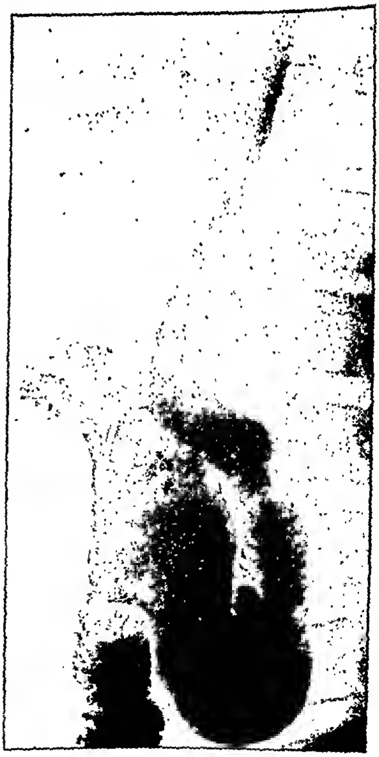


FIG. 1.—Appearance of œsophagoduodenal junction fourteen days after operation showing smooth passage of meal into duodenum and jejunum.

There are many methods of contraception, some of which are admitted to be injurious and others which are apparently harmless on each separate occasion, but which may not be so innocent either directly or indirectly when practised over a long period. The various methods fall under the following heads: (1) Chemical spermaticides; (2) occlusive pessaries; (3) permanent wear of metal contrivances—the so-called wishbone pessary, and the Graefenberg silver ring; (4) Douches, either spermaticidal or irrigation; (5) coitus interruptus.

(1) *Chemical spermaticides.*—A considerable amount of research, described and summarized by C. I. B. Voge in his "The Chemistry and Physics of Contraception", has been done upon the effectiveness of a great number of chemical substances—Voge lists about 147 chemical preparations made in various countries of the world, and a large number of different chemical agents used by manufacturers. The commonest of these substances are boric acid or borates in 44 preparations, chinosol (38), carbon dioxide in foams (34), lactic acid (21), quinine (19), alum (13), acetic acid (11), organic compounds of mercury (5).

The vehicles used are mostly cocoa butter which contains 40% stearic acid and 30% oleic acid.

It is probable that little harm is done by any of the chemical methods now in use. Occasionally there may be minor irritation of the vaginal mucosa, or absorption of quinine, but there is no evidence that these are serious in any appreciable number. We find severe vaginitis equally in all women whether they are young, old, virgins or married women with or without the use of contraception.

(2) *Occlusive pessaries and sheaths.*—The Dutch cap and Stopes cap are rubber obturators. The first occludes the vagina, and the second is a cap fitted over the cervix. The Dutch cap carries a charge of spermaticidal jelly on its upper surface, and may be regarded more as a vehicle for the spermaticide than an actual obturator to the upward passage of spermatozoa. It is probable that the Dutch cap is the most efficient, the easiest to use and least harmful of any method.

(3) The Graefenberg silver ring and the gold wishbone pessary are worn for some weeks or permanently in the uterine cavity. Their effect is to produce very early abortion rather than to prevent conception. As they are foreign bodies in constant contact with the endometrium it is obvious that they are liable to cause pressure ulceration and infection. I have seen two cases of acute salpingitis associated with the wishbone pessary. Moreover, the Graefenberg ring is by no means a certain contraceptive for I have delivered two women of full-term babies with the ring *in utero*. While there is almost universal condemnation of the wishbone pessary there are still a few who advise the use of the Graefenberg intra-uterine ring. If it were reliable there might be something to be said for it, but as it is not only unreliable, but also acts by producing the morbid process of abortion it cannot even be classed as a contraceptive because conception takes place in the tube. It is an abortifacient, and therefore its use is strictly illegal, just as the use of any other instrument for this purpose. On one occasion I found a silver ring embedded in the cervix, and on two other occasions had some difficulty in removing one from the uterine cavity. Retention of a foreign body inside the uterus offends against the basic principles of physiology.

(4) *Douches.*—The function of the post-coital douche is expected to be spermaticidal, but if of any value it is probably as an irrigation. As spermatozoa are found within the cervical canal within fifteen minutes of ejaculation, it is clear that douches are uncertain contraceptives. The materials in common use are water, soap solution, vinegar and hypertonic salt. Of these the most lethal agent is water. The occasional douche after coitus is harmless as well as useless.

(5) *Coitus interruptus* is a common practice, aimed at withdrawal by the male a few moments before ejaculation; for obvious reasons it is unreliable and is baneful to the woman. Apart from being unreliable it is bad because it usually deprives the woman of the orgasm. She is thus left in a state of unresolved pelvic congestion, which I believe is the cause of local troubles such as menstrual difficulties, but chiefly because it leads gradually to a nervous state which manifests itself in the shape of various neuroses. In one of the chief of all the natural functions she is left defeated and deprived. The cumulative effect of many repeated occasions must have a noxious effect on her whole physical and emotional organism.

Late results of contraception.—It is generally agreed that there are reliable methods of contraception which, by reason of the actual method, exert no injurious physical effects whatever.

Let us now consider whether a normal woman suffers from being prevented from conceiving, and passing through pregnancy and labour, or is deprived of any useful physiological influence by interference with the normal act of coitus.

Though there may be little or no harm to the woman due to each act of contraception at the time, it is possible that its long-continued practice may exert harmful effects.

It is alleged (1) that contraception prevents the benefits which undoubtedly occur from child-bearing. Where a normal married woman wilfully remains nulliparous during the whole of her reproductive life we all agree that she has lost some physiological stimulus apart from all the joy that a family of children will bring her. It is, however, only a very small number of normal couples who practise contraception throughout their married lives.

begetting offspring, its frequency, even in the generations immediately following, would be practically unaltered, for the condition is almost entirely transmitted, and concealed, by the (normal) heterozygotes. Similar measures would almost wholly eliminate a heterozygous condition, but it would reappear and rise to its former level in later generations, owing to mutation.

It may be noted, however, that the physician can give one useful piece of advice to members of a family in which a recessive defect is inherited: that it is more dangerous for them than for other people to marry near relatives, as the chance of bringing together two heterozygotes is greatly increased thereby. At the frequency just discussed, when 2% of the population are heterozygotes, the chance that a given heterozygote shall marry a person who is also a heterozygote is 1 : 49 against, if the marriage is not with a relation; but it is multiplied seven times if the marriage be with a first cousin.

Evidently it will be useless to apply general eugenic measures to the elimination from the population as a whole of defects due to single genes, though it may be right and proper to advise birth control to prevent the appearance of such conditions among the immediate descendants of affected persons. This is quite practicable for those which are heterozygous manifestations, but the only recessives for which it is so are those due to genes carried in the differential region of the X-chromosome: those showing total sex-linkage in X.

Such a condition as recessive retinitis pigmentosa (the form unassociated with deafness) is inherited in this way. No man can transmit the disease unless he himself be a sufferer, and he will do so to all his daughters and none of his sons. Affected women are very rare, since they must be homozygous. Heterozygous women, the "carriers" who receive the gene in single dose, transmit it to half their children, the sons develop the disease while the daughters are again "carriers." Thus the sisters of an affected patient can be told that for them there are two alternatives. That is to say, should they marry, either half their sons will be affected and half their daughters will be carriers, or else none of their children will suffer from the disease nor can any transmit it. For such a woman, the probability of these two situations is exactly equal, and she may well feel that she should not beget children. The chance is of course one in four that any woman with an affected uncle (but no affected brother) is a carrier.

Until recently, the same unsatisfactory dilemma faced women closely related to sufferers from hæmophilia, the most famous of the sex-linked recessives. However, Andreassen, working in Denmark, has shown that by appropriate measurements of coagulation time, heterozygous women can be distinguished from true normals. This is a considerable advance. The sisters of hæmophiliacs can now be told definitely that they should not have children or, alternatively, that they can do so with safety.

So far as the use of birth control is concerned, partially sex-linked conditions are in the same position as those transmitted by the autosomes.

This discussion has so far been limited to defects controlled by single genes. These are each rare, though in all they constitute a formidable problem. One very different problem requires at least brief mention here: that of mental deficiency. This of course may be caused in many ways but, apart from the effects of specific disease, it is strongly inherited. In certain instances single genes are responsible, as in phenylketonuria (which is a simple recessive), but in general it has a multifactorial basis. Apart from its high frequency, mental deficiency differs in two ways from the situations so far considered. First, there is a tendency for mental defectives to beget more, not fewer, children than normal, and secondly, multifactorial disorders are much more susceptible to the effects of selection than are unifactorial ones. Consequently, if it were possible to prevent all mental defectives from having children, the frequency of the condition could be materially and quickly reduced. The desirability of birth control measures, and the difficulty of their application, in individual instances of mental deficiency, are sufficiently obvious to need no elaboration.

It will be seen that it is possible to come to certain fairly definite conclusions in regard to those instances in which birth control can reasonably be recommended on genetic grounds. Lists of defects inherited respectively as heterozygous and recessive conditions are available in the textbooks, but special care should be taken in regard to those in which it is stated that the gene is variable in expression or in which the heterozygotes are sometimes affected and sometimes normal. Provided with such data, a practitioner may be able to help a number of patients who require information on birth control on account of inherited disease in their family.

Mr. Aleck Bourne: *The medical aspects of birth control.*—An objective study of birth control from the medical point of view is an inquiry into how far the practice may be harmful or beneficial to the woman. The whole subject is so beset with moral and religious prejudice, and more and more with social and political anxieties that it is not easy to persuade many people to look only at the mental and physical effects it may have upon individual women. Let us examine these in the light of experience and consider first what harm may be suffered.

It is possible that the woman may be injured more or less by the method adopted, either on any given occasion or as a result of long-continued practice, or it may be that the actual prevention of pregnancy or the destruction of the semen will ultimately impair both her physical and mental health.

dyspareunia for which no physical signs can be found, frigidity and refusal. Almost inevitably neuroses of various kinds develop, the woman, driven by her husband, seeks abortion with its risks, she feels self-guilt and often remorse, and a marriage of hope and affection is turned into a squalid bickering partnership.

This is a gloomy depressing story, but all of us who have practised gynæcology over many years know how common and true it is.

Contraception when wisely used can prevent all this. It has arrived as the logical result of the change in our modern times, and will continue because mankind is in the grip of an evolution which is blind and merciless. Those who would abolish contraception must abolish the circumstances which have brought it into being.

REFERENCES

Bacsich P., Sharman, A., and Wyburn, G. M. (1945) *J. Obstet. Gynec.*, 52, 334.
Green-Armytage, V. B. (1943) *Proc. R. Soc. Med.*, 35, 105.
Voge, C. I. B. (1933) The Chemistry and Physics of Contraception. London.

Dr. Kenneth McFadyean: I am asked to approach this subject from the point of view of the general practitioner but, as that species includes a great many variants, I shall perhaps be wiser to claim only that I am expressing the views of one general practitioner.

I never cease to be amazed at the ignorance of contraception displayed by many members of our profession. The causes of such ignorance are easy to recognize but I remain amazed at the continued existence of such causes. First the ignorance is due, in part, to the considerable bias of fanatical religion, the authority of which will not allow its adherents to have any contact with, or form any scientific opinion with regard to, the subject. It is profoundly to be regretted that in a matter seriously affecting the health, morality, and happiness of a nation some religious denominations should obstinately maintain an attitude so grossly at variance with the practice of most of their members and all their priests, for celibacy is but one method of birth control. The second and more important cause of such ignorance is to be found in the absence of instruction to medical students in the teaching hospitals. I am not disturbed by the absence of instruction in medical textbooks for, as Trotter was once heard to say, textbooks are invariably wrong.

The intelligent effort to make the knowledge of wise and safe contraceptive methods generally available to all sections of the community is modern, as modern as liberal political philosophy. It is, however, wrong, due either to ignorance or malice, to suggest that this modern social movement is a direct consequence of liberal-minded propagandists. That is indeed putting the cart before the horse. The Rev. Thomas Malthus published his "Essay on the Principles of Population" in 1789 but it was not until 1823 that Francis Place published his "Contraceptive Handbills" and not until the famous trials of Bradlaugh and Truelove in 1877 and 1878 that any really great impetus was given to the movement. The Bradlaugh trial was largely responsible for the formation of the Malthusian League in 1877, nearly one hundred years after the publication of the "Essay". Francis Place, probably influenced by the writings of Benjamin Franklin, foresaw that a more general knowledge of contraception would result not only in a fall in the birth-rate but in many other indisputable benefactions such as earlier marriage, less prostitution, and less sexual abuse and vice of all kinds.

Having narrowed the field of birth control to that of conception control, I would suggest that this is one of the subjects, the total of which is small, upon which the general practitioner can speak with authority, for he probably has a wider experience of the subject than most other people. Let me quite shortly give my views on the methods of such control that have come within my experience during the last thirty years in an extensive middle-class practice. No one will deny that the control of conception is a frequent necessity on grounds of ill-health, both physical and mental. The methods employed to-day in this country are, first, that of "living apart." In most cases this is an intolerable burden to one or both of the partners in the marital union, particularly if they are both young. It is surely doubtful whether this method is ever advised in the case of young people, except by the authority of religious instruction. In one case, where I saw the Church's advice acted upon in this manner, it had the most disastrous physical and moral results for both parties. In this connexion let me say that there is far too little contact between our profession and organized religion in regard to every conceivable sexual difficulty that arises in human life, particularly in the marital state. Indeed the time is long overdue when every person entering the marital union should receive, in addition to religious instruction, advice from members of our profession in regard to the anatomical, biological and psychological differences between the sexes.

Secondly, there is the method of post-coital expulsion and douching, a method which is both unreliable and fraught with many dangers to the woman.

Thirdly, there is the method of female passivity, an unnatural, unhappy and unreliable method baser than prostitution.

Fourthly, we have "withdrawal," a method fraught with the greatest risks from the point of view of successful contraception and one which cannot be advised by any but a person ignorant of the physical and psychological mechanism of coitus.

(2) That contraception may be a cause of sterility in future years. On this there is no firm knowledge, but it is likely that a doctor with a strong prejudice against its use may be led, without evidence, to associate sterility with pre-existing contraception. After having seen even very few consecutive cases of sterility he may form a strong impression that the two are associated, but it is highly unlikely that the ordinary methods of sheath, Dutch cap or chemical pessaries can damage either the function of ovulation or the process of fertilization in future years. An exception of course to this must be the use of the internal pessaries—Graefenberg ring and wishbone—which can cause infection and salpingitis, and also long-continued coitus interruptus which may interfere with ovulation by repeated unresolved congestion of the ovaries.

(3) That certain methods, perhaps all, can and do prevent the absorption of a chemical body from the seminal fluid which has a stimulant action on the full development and maintenance of the female genital tract. Green-Armytage states that, after injection of human semen into immature rats and rabbits, "full development of the female genitalia is due to the absorption by the vagina of hormones from the human semen, and that this hormone is probably testosterone or a hormone allied to it." From this observation he states: "the deduction being that anything or any method which prevents, retards or alters the normal degree of physiological absorption of human semen from the vagina carries with it during the early months and years of marriage the risk of future sterility from failure of uterine development and endocrinal asynchronization."

If Green-Armytage's observations are correct, and his deduction is logical, it is obvious that all forms of contraception cause a serious loss to the woman, but I must add that he is well known to be a very strong opponent of birth control.

Bacsich, Sharman and Wyburn have repeated the work of Green-Armytage and, in addition to human semen, have also injected immature animals with testosterone. They found no changes in the uterus or vagina, nor ovarian stimulation as a result of semen injections into immature rats. Guinea-pigs showed no vaginal reaction and only "slight non-significant uterine hypertrophy" and no ovarian stimulation. Testosterone produced hypertrophy of the clitoris, some vaginal reaction and uterine enlargement.

These observations are supported by the common clinical experience of finding normal development of the whole genital tract, both of structure and function, in virgins of all ages, and the small undersized uterus and smooth vaginal mucosa in married women, anxious to have children, who have never used contraceptives. The evidence therefore that prevention of the contact of unaltered semen with the vaginal mucosa leads to failure of genital development is so far flimsy.

The very large majority use contraception to delay or space their pregnancies. We must conclude therefore that harm to the woman or couple does not follow the methods used except coitus interruptus and permanent intra-uterine pessaries. Nor is it likely that the woman suffers any physiological loss from interference in absorption of some hypothetical substance in the semen. She will, however, suffer a loss of fulfilment if she voluntarily deprives herself of all child-bearing, and a lesser loss if the family is limited to one or perhaps two. Here the family unit, if it consists of only one child, also loses something which moderate, or even large families enjoy, provided economic circumstances are adequate.

Benefits of Contraception

Having discussed the possible harmful effects of contraception what is there to be said for the credit side?

The power to prevent child-bearing is a boon to some women where it is used only to avoid too frequent pregnancies, in other words, to space their children. Individual circumstances of personality, character and economics of course differ, and no rules can be laid down, but, in general, it is right to say, that where contraception is not used to prevent all children, but only used, not so much to limit the number, but to space them, it is wholly good.

I have spoken of how far the methods and effects of contraception may damage the woman, but equally we should ask, with the same anxiety, how far unlimited and annual child-bearing will also injure the woman physically, or indirectly disrupt her marital relations. We all know that some women are able to have many children at frequent intervals without any harm whatever. We are reminded of the Victorian days when large families were common and our grandmothers lived through the happy content of their years. But the epoch has changed, and, though we may deplore it, the change is inexorable and irreversible. The impact of a new way of life and a new set of economics has fundamentally altered the attitude of mind of womanhood to child-bearing.

The state of the woman of to-day who has rapidly repeated pregnancies must therefore be considered, not in terms of the Victorian age, but in the light of the circumstances of our own times. The result of the influence of modern conditions is that the majority of women, both of the middle and working classes, who become pregnant year after year, not only lose the happiness of their married lives, but become spiritually and emotionally celibate.

The physical act of coitus becomes an occasion of fear and apprehension. Thus is lost the libido on which much of married happiness during the early years is founded. This often leads to

Finally we must recognize that all our efforts have failed to prevent the number of illegitimate births from rocketing, at least in the recent war, and immediate post-war, periods. Before the war the annual figure of such births in this country was fairly steady at 25,000 but in 1942 it had risen to 40,000 while last year it rose to over 50,000. I am not at the moment prepared to advocate the propagation of conception control among unmarried women but opposition to such a procedure comes ill from those who are insistent upon the male sex being given every conceivable protection against the possible consequences, of another kind, resulting from illicit sexual communication.

Sir Travers Humphreys: The practice of contraception is not unlawful. Marriage is a contract, of which consummation is an implied condition: and non-consummation due to impotence has been for centuries a ground for annulment. Last July the Court of Appeal held that a marriage is not consummated unless penetration is followed by emissio seminis; thus, a wife may seek annulment if the husband wilfully refuses intercourse except with the use of a rubber sheath. It will be interesting to learn the views of their Lordships when the converse case arises—if the wife after full connexion and without the knowledge of the husband excludes the chance of pregnancy by the use of a syringe, will the husband be entitled to a decree?

Abortion is undoubtedly criminal; therapeutic necessity is the only ground on which abortion can be approved or excused, and I sincerely hope that neither by Parliament nor by the judges will the decision of Mr. Justice Macnaghten in 1937 be altered. The matter is not so much one of law as of the good sense of the jury. The test is, does the doctor honestly believe that it is absolutely essential in the interests of the woman's physical or mental health to perform the operation? Here the doctor is put in the same place as an operating surgeon in hospital. To cut off a leg is a serious assault, and the only reason such an act is not criminal is the interest of the patient's health and life. The patient's personal wish affords no defence in law.

As to sterilization of the male, I do not know enough of the manner of performing the operation to enable me to express an opinion as to its legality. If it involves the maiming of the man it may well be unlawful and the consent of the patient will not excuse the practitioner since no man can lawfully authorize his own maiming unless the operation in in the interest of his health.

Mr. Reynold Boyd deprecated the inclusion of discussion on abortion at a meeting on birth control which, to the majority of people, meant contraception. He asked about the legalities of voluntary male sterilization by vaso-ligation for convenience and not specifically for health reasons—for instance of a man with 4 children and a wife of 43 where fear of further pregnancy was ruining the marriage. He thought the original law referred to castration and not ligation which in any case was reparable. Finally he thought that the recent definition of emissio seminis should be revised for divorce purposes.

Mr. V. B. Green-Armytage began by referring to the death of Dr. Pangloss in Voltaire's Candide where he, though in dire straits, curses Candide and says all is well, all is for the best. Is all well to-day, when at many Centres throughout the country young unmarried girls can be fitted with birth-control gadgets so that they can "walk out" with their boy friends? The spread and underground percolation of such birth-control information has resulted in an immeasurable degree of promiscuity, illegitimacy, venereal disease, abortion and subsequent sterility.

The speaker then continued: As a result of the use of birth control for any length of time before conception of the first baby, there is an ascending spiral of primary sterility in this country, which so often leads to the divorce courts.

It is one of the first axioms of eugenics that without numbers there can be no variation. Therefore it is not to be wondered at that no genius has been born to this or any other country during the last 40 years.

The pernicious Baldwinian "Safety First" doctrine of young married people to-day, has resulted in vast numbers of frustrated husbands, inhibited wives, perverts, introverts, nancies and pansies. Hence psychiatrists have come into their own.

Another result of the one—two family is that we are fast becoming a nation of old people whose old age pensions will have to be paid for by a groaning and complaining body of youth.

It is my belief from what some of the medical speakers have said that they have in mind to stimulate the start of a new diploma for our graduates as well as post-graduates to be called the D.D.C.F.—that is the Diploma for Dutch Cap Fitting. These people who advocate unremitting birth control are a danger to the State and our Empire. Indeed all is not well. Therefore let us with Candide "cultivate our garden." Mr. Bourne referred to some experiments of mine which he states have been disproved by another worker. May I say that this research has since been repeated using homologous semen with positive results in 80 per cent. of cases, and will be published shortly. They show that there is a principle or agent in the semen which promotes growth, indubitably.

Mr. Anthony W. Purdie asked for further information on the legal issues involved in the sterilization of the husband for conception control. In reply to a previous speaker Mr. Justice Humphreys had

Fifthly, there is the male contraceptive sheath. This is a comparatively old method, dating from the linen sheath in use in the sixteenth century, but it is open to the charge of unreliability and to the serious objections that it separates the partners to the act and deprives the women of the influence of seminal fluid. I refer to the seriousness from the physical and æsthetic point of view, not from the legal point of view.

In the sixth place is the use of chemical contraceptives and the wearing of an occlusive pessary by the female. Some authorities apparently regard the occlusive pessary as having originated with the Mensinga Cap in the '80s but Marie Stopes found a German description as early as 1838. She regards it as but a modern version of the five thousand years'-old Egyptian "Barrier". In more modern times we find the use of half a lemon advised by Casinova, in the latter part of the eighteenth century.

The use of chemical contraceptives alone is certainly not reliable. The use of an occlusive pessary alone is probably more reliable but a combination of the two is in my experience infallible, provided the woman is properly examined and provided with appropriate instruments and advice by the medical practitioner. For over thirty years I have advised none other than this method for regulating conception. It should be remembered that this method is not advised so much as a method of permanent or even indefinite contraception but as a method for regulating conception. So far as my experience goes it is utterly devoid of any reasonable objection. It is infallible; it is non-injurious to either party; it does not interfere with the anatomical or aesthetic relationship of the partners. All it attains is the prevention of conception. Many authorities, including Van der Velde, believe that the presence of seminal fluid in the vagina has some not inconsiderable influence on the woman. If this belief is well founded, modern contraception does not mitigate against such influence.

One must pass some comments on the supposed objections to this method. I am not concerned with the irrational authoritarian objection of certain religious denominations, for such bodies do not in fact object to birth control, or even conception control of the more undesirable kind; they only object to the easy and pleasant method of conception control and would add further trial and tribulation to those already afflicted, with no justification, and no solace to offer, other than that "these things are sent to try us". The same might be said of earthquakes or senility, with a great deal more reason, for as yet we have little to offer to combat such evils.

I have never seen such a method, used with discrimination, result in harm to either party. I have never seen it result in sterility, even when it has been practised for some years after marriage; that it may result in non-consummation is another matter. I have never seen a "Malthusian Uterus" and am not prepared to discuss such nonsense as the production of uterine fibroids, carcinoma uteri, urethral caruncle or even chronic appendicitis by this method of contraception. Not only have I never seen any of these consequences but never has any disease in the female pelvic organs, in my practice, been attributed by a consulting gynæcologist to this or any other method of contraception. Perhaps my consultations have been too few.

Admittedly in years gone by one did see cases of vaginal irritation due to cocoa butter or quinine. Such cases never had serious results nor ever resulted in chronic inflammation. These minor troubles are rapidly disappearing with the advent of latex rubber occlusive pessaries and more modern non-irritant chemical contraceptives. When one reads some of the biased views expressed, even by members of our own profession, in regard to the injurious results of such practices, one wonders whether those holding such views are blind to Nature's failure to sterilize the human penis and to the aggravation of its condition by the dirty clothing and dirty occupations imposed upon men by civilization.

I am strongly of the opinion that within the period of my medical experience inflammatory and ulcerative conditions of the vagina and cervix uteri have shown a great reduction in numbers. If I am right in this opinion, it is possible that one of the factors producing such a result may be the more widespread knowledge of advisable methods of contraception.

Next comes the question of abortion. The intense suffering and shocking loss of life through illegitimate abortion have always horrified me, particularly as I have always believed that these tragedies, in the majority of cases, were to be found in married women, already mothers of one or more children. Many years ago I shocked some of my colleagues by publicly advocating the legalization of abortion. It seems likely that the dissemination of knowledge of contraception has reduced this wastage of life. Carlyle's crabbed satirist said "A judicious man looks at statistics not to get knowledge but to save himself from having ignorance foisted upon him". Statistics prove nothing. They are too often but a feeble expression of a doubtful opinion. However, here are statistics which *may* support an opinion firmly held. In the Registrar-General's reports deaths due either to abortion, or to causes associated with abortion, in 1930 were 588, by 1935 the figure had fallen to 464 and by 1940, the last year for which I can find the combined figure, the number had fallen to 268. It should be noticed that these figures cannot be affected by the discovery of penicillin. If I am right in thinking that the regulation of conception is one factor in this welcome improvement, then I would gladly see some degree of compulsion introduced in the dissemination of contraceptive knowledge.

Section of the History of Medicine

President—Sir ARTHUR MACNALTY, K.C.B., M.D.

[*October* 2, 1946]

The Evolution of Preventive Medicine in England

PRESIDENT'S ADDRESS

By Sir ARTHUR SALUSBURY MACNALTY, K.C.B., M.A., M.D., F.R.C.P.

IN the twilight of civilization, when primitive man lived in caves and encampments, and when isolated groups of families merged into tribes for purposes of security, defence and offence it is possible to trace the beginnings of preventive medicine. The biologist tells us that in the earliest stages of human existence man must have perceived some glimmerings of the need for health preservation, which pointed out steps of quest or avoidance in the interests of self-protection. The perils of hunger and thirst, the poisonous nature of certain foods and waters, the fatality of malarious regions, the dangers of extreme heat and extreme cold, the destruction wrought by floods and drought, outbursts of infectious disease and pestilence in the tribe: these are examples of conditions inimical to health, which must have been familiar to our primordial ancestors, and must have early inclined them to desire to escape disease and to devise measures for doing so.

Then, again, communal effort in agriculture promoted good nutrition, and provision was made against scarcity and famine by the erection of public storehouses for food distribution in the common interest. Water supply was always of imperative necessity, and this led to the invention of mechanical devices for its conduction and storage. At first the necessity on grounds of health for an unpolluted water supply was not realized, but the religious veneration for rivers, streams and founts must have promoted this to some extent. River-gods and naiads were the guardian deities of running water, and deliberate wilful pollution of the river that gave drinking water was impiety and sacrilege. The care directed to water supplies led on to systems of drainage, primarily, for the protection of agricultural land and afterwards for the removal of dejecta. The discovery that accumulations of household refuse and filth were of value as manure led to the removal of the insanitary "kitchen midden" about the homes of our ancestors, and scavenging came into use with consequent benefit to health.

EGYPTIAN AND GREEK MEDICINE

As for the prevention and treatment of disease in primitive times, sickness, especially epidemic disease, was regarded as a punishment from the gods or tribal deities to be expiated through the agency of witch-doctor or priest. It cannot have been long, however, before observation taught men that contagion played a part in the dissemination of epidemics.

"Latona's son a dire contagion spread,
And heap'd the camp with mountains of the dead."
Iliad, Book I.

been emphatic that the operation was illegal, and that a doctor who performed such an operation would do so at his peril. The hypothetical case, however, which prompted this statement of opinion was one in which the operation had been proposed merely on the grounds of the couple's already having a sufficiency (for them) of children. But a request for the sterilization of the male was sometimes made in quite different circumstances. Take, for example, the case of a woman suffering from organic heart disease who had already two or three children. As doctors we considered that she should have no further children because of the organic disease of the heart. The normal recommendation would be that she should be sterilized. In these circumstances, however, a husband from time to time asks that he—rather than his wife—should be sterilized on the grounds that his wife has already suffered enough. In such a case what would be the legal position if his request were granted? Would a doctor sterilizing a husband under similar circumstances be likely to run into legal trouble?

Dr. Letitia Fairfield said that there were many circumstances which made it unwise to sterilize healthy persons on request. If for example, a woman had such serious heart disease or tuberculosis that she was permanently unfit for child-bearing and was unfit even to undergo a sterilizing operation herself, she was obviously liable to die before very long. Suppose the husband who had been sterilized then wanted to remarry—what then? Would it be to his ultimate good or that of his future wife that the surgeon had acceded to his request? Nor were motives behind the "requests" always altruistic. She could recall the case of a man who was living with a mentally defective girl and greeted the social worker who called to make enquiries with the remark "You needn't worry about her having a baby, I had an operation done in S. America so that I can enjoy myself when I like and not bother about the results." In the U.S.A. she met two—or more—surgeons who had informed her that they had seen such tragic results from sterilizing healthy people that they had decided to abandon the practice.

As for the recent legal decisions in birth control and consummation of marriage, as described by Mr. Justice Humphreys, it seemed to her that it left the law in a chaotic condition. The decision of the Court of Appeal that valid consummation depends on a quite unprovable event—(*an ejectio seminis*) is highly unsatisfactory. So was the decision of Mr. Justice Jones in the Divorce Court, for it was apparently now possible for a wife to obtain an annulment if her husband had been sterilized without her knowledge, or used (for example) two of the commonest methods of male contraception, but gave no remedy to the husband whose wife had been operated on or who used the common methods of female contraception. It was possible that both these decisions were made under misapprehensions of physiological facts, but in any case the legal position should be clarified without delay.

Dr. Alexander Kennedy: Apart from a few uncommon conditions, mentioned by Dr. Ford, in which the mode of inheritance was understood, the only group of any numerical consequence in which birth control could be advised as a eugenic measure was the mentally defective group in which the inheritance was multifactorial. There was evidence that among high-grade defectives who are free in the community and able to procreate, the intelligence level of the offspring tends to be at the average of the parental levels. Although limitation of the families of this group was most desirable, it was the daily experience of psychiatrists that attempts to use birth control appliances by such patients were very often unsuccessful The same was true of many neurosis-prone and psychopathic patients in whose condition inherited factors were almost equally probable and who were impulsive and incompetent in managing their affairs. Birth control technique in this group was likely to be unsuccessful for exactly the same reasons. There was thus a tendency for birth control to limit the families of those who were able to pass the test of competence with the apparatus, while merely creating a sense of false security in the less capable and stable members of the community. Few would doubt the value of birth control methods in protecting vulnerable personalities from the extra strain of inopportune childbirth, but its value as a eugenic measure was probably very limited until the methods employed were more foolproof.

Dr. Edward F. Griffith could not agree with what Mr. Green-Armytage had said. He challenged him to name a single Women's Welfare Centre in the country that taught young girls contraceptive methods so that they could go down the street and have affairs with their boys. Such an assertion was a gross misrepresentation of the whole purpose, not only of Women's Welfare Centres, but of contraception in general. It was true of course, that contraception could be abused, but so could any other scientific discovery. Contraception and abortion were entirely different and should never be considered in the same category. Abortion was a destruction of life, whereas contraception merely prevented fertilization—the one was destructive and the other was essentially constructive provided that it was used for the purposes that the other speakers had already indicated, i.e. proper spacing of children and the achievement of mutual harmony in marriage. From his own experience both as a general practitioner for fifteen years and as a specialist in marriage problems for ten, he agreed entirely with what Dr. McFadyean had said. Contraception, one of the most valuable discoveries of the age, *had* come to stay. Our duty was not to condemn it but to see that it was properly used.

THE EIGHTEENTH CENTURY

It was in the succeeding century, the eighteenth century, that a galaxy of medical practitioners appeared in the firmament of Medicine, whose clinical investigations form the basis of modern preventive medicine.

Before touching on their discoveries mention should be made of a non-medical research worker, whose studies contributed largely to advances in physiology and preventive medicine. This was the Rev. Stephen Hales (1677-1761). His *Vegetable Staticks* (1727) marks the early stages of our knowledge of the physiology of plants; his *Haemastaticks* (1733) treated of blood-pressure and circulation of the blood. Besides a work on dissolving stone in the bladder, he wrote in the *Philosophical Transactions* on ventilation, electricity, analysis of air, &c. He also invented ventilating machines and machines for distilling sea-water and for the preservation of meat.

It was, as I have just said, in the practice of clinical medicine that the science of preventive medicine now began to emerge, and it is a remarkable feature of this eighteenth-century work that it was done by men working independently at their individual problems, and, for the most part, ignorant of the others' investigations. In epidemiology they were the disciples of Thomas Sydenham, observers of the clinical features of epidemic disease, the influences of external environment, the paths of contagion and infection, and the effects of climate and season.

> "Huxham of Totnes studied typhoid, typhus, scurvy and diphtheria; Richard Mead, plague and scurvy; the illustrious Heberden, diphtheria, angina, chicken-pox, night-blindness, smallpox and 'epidemical colds'; Fothergill, epidemic sore throat; Haygarth of Chester, smallpox, typhus and rheumatic fever; Willis, epidemic diphtheria, typhoid and puerperal fever; and Withering of Shropshire, scarlet fever, heart disease and tuberculosis" [4].

In connexion with the plague and sweating sickness of the sixteenth century, methods of medical notification including Bills of Mortality[1], of isolation of infectious persons and contacts from the community, of fumigation and disinfection had been introduced. These methods were now applied with success to other forms of infectious disease.

The eighteenth century also saw the beginnings of university education in preventive medicine [5]. In 1786 Johann Peter Frank was appointed director of public health of Austrian Lombardy, and his international fame led to the creation of the first Chair of Public Health in Edinburgh University. Dr. Andrew Duncan, who became Professor of the Institute of Medicine in Edinburgh in 1789, began in 1795 a series of lectures on forensic medicine, including "medical police", in which he dealt with both personal and environmental health. In 1798 Duncan presented a memorial, as the outcome of which in 1807 George III granted a commission creating a professorship of medical jurisprudence and medical police "as taught in every university of reputation on the Continent".

ADVANCES IN OBSTETRICS AND CHILD WELFARE

In obstetrics too further advances were made, for the high rate of mortality in childbirth began to excite medical if not public concern. William Harvey in 1651 had produced *De Generatione Animalium*, which discussed the anatomy and physiology of the human embryo and placed the study of midwifery on a scientific basis. Peter Chamberlen's discovery of the obstetric forceps by the eighteenth century was no longer a secret, and Dr. John Mowbray and Mr. Edward Chapman were using it in general practice. Sir Richard Manningham in 1739 established a lying-in hospital in the Infirmary of the Workhouse of St. James, Westminster, where instruction was given to medical students and midwives [14].

---

[1] The London Bills of Mortality were records of burials and baptisms kept by the Company of Parish Clerks.

Such a concept must have been known to the Egyptians, for Egyptian medicine is regarded by Hebrew and Greek historians as the original source of medical knowledge. According to Herodotus, Egyptian medicine was specialized to a degree comparable only to that seen in the United States to-day. He wrote:—

> "The art of medicine is thus divided amongst them: each physician applies himself to one disease only and not more. All places abound in physicians; some physicians are for the eyes, others for the head, others for the teeth, others for the parts about the belly and others for internal disorders" [1].

"Moses was learned in all the wisdom of the Egyptians", and has been rightly termed the first Minister of Health, for the Book of Leviticus is a compendium of sanitary law. He enforced compulsory notification, and set out in detail systems of isolation and of disinfection of patients and their dwellings. Assyria had a Code of Medicine (the Hammurabi Code), while Greek medicine in many of its practices was more advanced than British medicine in the nineteenth century. "Like everything that is good and durable in the world, modern medicine is the product of the Greek intellect", said Osler. The practice of hygiene, life in the open air, sunlight-therapy and a balanced dietary were familiar to the Greeks in the fifth century B.C. They had the sun-temples of Cos and Epidaurus, the health principles of Hippocrates, Alcmaeon and Empedocles, and Greek medicine was active and progressive, until it became doctrinal in Galen's interpretation of the Hippocratic writings. Even when the Arabians disseminated Greek medicine to Western Europe, the teaching intended to stimulate progress paradoxically retarded it through its very authority. There was one great exception: Offspring of Greek Medicine, by the eleventh century Salerno was the most celebrated medical school in Europe. It taught hygiene and preventive medicine, and issued the first regulations requiring qualification and licence for medical practice.

PUBLIC HEALTH IN MEDIÆVAL ENGLAND

Pestilence has always been a stimulus to public health. In England leprosy brought about the establishment of leper hospitals by the ecclesiastical authorities, the beginnings of our hospital system, and methods of notification and isolation. Plague demonstrated the necessity of sanitation in the hovels of the poor. The first Sanitary Act was passed by the English Parliament at Cambridge in 1388; it was followed by quarantine laws, by the appointment of scavengers, by sanitary watchmen, and by penalties for the concealment of infected persons.

The Renaissance and the knowledge of Greek authors produced great medical schools at Padua and Montpellier, and the Oxford humanists brought the new learning to England. Linacre organized English medicine, and helped to found the College of Physicians in 1518, of which he was the first president. Thomas Vicary's work in uniting the Corporation of Surgeons with the Barber-Surgeons and in promoting the teaching of anatomy and surgery led immediately to progress in British surgery. Sir Thomas More, as I have shown elsewhere [2*a* and *b*], was a great health reformer. We have to wait until the nineteenth century for a man of equal vision and breadth of view to appear in Edwin Chadwick. Other pioneers in public health of the Tudor Age were Sir Thomas Elyot, diplomatist and author, William Bullein and Andrew Boorde. From Padua Vesalius, Fabricius and William Harvey brought new learning and perception into the healing art. The golden key of the Renaissance unlocked doors which led to a wonderful domain of natural science and experimental medicine, whose confines to-day are still unlimited and unexplored.

THOMAS SYDENHAM AND OTHERS

The seventeenth century saw the foundation of the Royal Society in 1662. Thomas Willis advanced medical knowledge, Daniel Whistler and Arnold Boot identified, and Francis Glisson, the morbid anatomist, gave the first scientific account of rickets, Christopher Bennet and Richard Morton described pulmonary tuberculosis; and the study of medicine and surgery, based on experiment and observation, went forward linked with discoveries in biology, comparative anatomy, chemistry and physics, which threw fresh light on the problems of health and disease.

Thomas Sydenham (1624-1689) reinterpreted the Hippocratic conception of epidemics and led the way to the domain of modern epidemiology. He renounced unsupported authority, dogmas and theories and went to Nature. "He laid down the fundamental proposition, and acted upon it, that 'all diseases should be described as objects of natural history' " [3].

THE EIGHTEENTH CENTURY

It was in the succeeding century, the eighteenth century, that a galaxy of medical practitioners appeared in the firmament of Medicine, whose clinical investigations form the basis of modern preventive medicine.

Before touching on their discoveries mention should be made of a non-medical research worker, whose studies contributed largely to advances in physiology and preventive medicine. This was the Rev. Stephen Hales (1677-1761). His *Vegetable Staticks* (1727) marks the early stages of our knowledge of the physiology of plants; his *Haemastaticks* (1733) treated of blood-pressure and circulation of the blood. Besides a work on dissolving stone in the bladder, he wrote in the *Philosophical Transactions* on ventilation, electricity, analysis of air, &c. He also invented ventilating machines and machines for distilling sea-water and for the preservation of meat.

It was, as I have just said, in the practice of clinical medicine that the science of preventive medicine now began to emerge, and it is a remarkable feature of this eighteenth-century work that it was done by men working independently at their individual problems, and, for the most part, ignorant of the others' investigations. In epidemiology they were the disciples of Thomas Sydenham, observers of the clinical features of epidemic disease, the influences of external environment, the paths of contagion and infection, and the effects of climate and season.

> "Huxham of Totnes studied typhoid, typhus, scurvy and diphtheria; Richard Mead, plague and scurvy; the illustrious Heberden, diphtheria, angina, chicken-pox, night-blindness, smallpox and 'epidemical colds'; Fothergill, epidemic sore throat; Haygarth of Chester, smallpox, typhus and rheumatic fever; Willis, epidemic diphtheria, typhoid and puerperal fever; and Withering of Shropshire, scarlet fever, heart disease and tuberculosis" [4].

In connexion with the plague and sweating sickness of the sixteenth century, methods of medical notification including Bills of Mortality[1], of isolation of infectious persons and contacts from the community, of fumigation and disinfection had been introduced. These methods were now applied with success to other forms of infectious disease.

The eighteenth century also saw the beginnings of university education in preventive medicine [5]. In 1786 Johann Peter Frank was appointed director of public health of Austrian Lombardy, and his international fame led to the creation of the first Chair of Public Health in Edinburgh University. Dr. Andrew Duncan, who became Professor of the Institute of Medicine in Edinburgh in 1789, began in 1795 a series of lectures on forensic medicine, including "medical police", in which he dealt with both personal and environmental health. In 1798 Duncan presented a memorial, as the outcome of which in 1807 George III granted a commission creating a professorship of medical jurisprudence and medical police "as taught in every university of reputation on the Continent".

ADVANCES IN OBSTETRICS AND CHILD WELFARE

In obstetrics too further advances were made, for the high rate of mortality in childbirth began to excite medical if not public concern. William Harvey in 1651 had produced *De Generatione Animalium*, which discussed the anatomy and physiology of the human embryo and placed the study of midwifery on a scientific basis. Peter Chamberlen's discovery of the obstetric forceps by the eighteenth century was no longer a secret, and Dr. John Mowbray and Mr. Edward Chapman were using it in general practice. Sir Richard Manningham in 1739 established a lying-in hospital in the Infirmary of the Workhouse of St. James, Westminster, where instruction was given to medical students and midwives [14].

---

[1] The London Bills of Mortality were records of burials and baptisms kept by the Company of Parish Clerks.

William Smellie, a Scot, who had learned his midwifery in Paris, settled in London, and as practitioner, teacher and writer advanced knowledge of his subject. He elevated the status of the man-midwife; introduced forms of technique for the measurement of the pelvis, safe use of the forceps, diagnosis and treatment of *placenta prævia*, and improved modes of version. Another Scot, William Hunter, was primarily an anatomist, but he was also a practising obstetrician. His methods were conservative, but they were eminently sound. Hunter's pupil, Charles White of Manchester, in his excellent treatise, *On the Management of Pregnant and Lying-in Women and the means of curing but more especially of preventing the principal disorders to which they are liable*, published in 1773, dealt with the general management and hygiene of childbirth, ante-natal supervision, and the cause and prevention of puerperal fever. By his hygienic methods—scrupulous cleanliness, fresh air, suitable temperature of the lying-in ward, dietary and disinfection—he claimed that he had never lost a patient from puerperal fever. These three men, Smellie, Hunter and White, so greatly advanced obstetrics that further improvement was impracticable until Simpson discovered chloroform anæsthesia and Lister antiseptic surgery.

Side by side with improvement in maternal mortality can be noted the beginnings of infant welfare in isolated attempts to control the high mortality of infants and children, which amounted in 1730-49 to as much as 74% of children born. Lettsom and Cadogan especially drew attention to the subject, set up "infant dispensaries" and advised on the care of infants.

The Foundling Hospital, aimed at stopping the exposure, desertion and murder of infants, was established by Captain Thomas Coram in 1739. The financial difficulties of the hospital, the great demand for places and the terrible records of the deaths of children in the Bills of Mortality induced the Governors, of whom Jonas Hanway was one, to appeal to Parliament for help. From June 1756 to Ladyday 1760 the Hospital received all children brought to it, the cost being defrayed by a Treasury grant. After that it reverted to a private charity. Hanway also inspired the important Act of 1767 which boarded out parish children in London with carefully selected cottagers in the country. Howlett [13] estimated that the London burials were reduced by 2,240 in the first year and, that, allowing for the children who returned to London and died there, the annual average reduction in the London burials was 2,100.

Lettsom and others also advocated improved standards of nutrition for the population at large, and urged the restriction of or abolition of spirit drinking, which was then a cause of high mortality and a blot on our national civilization. The College of Physicians and numerous grand juries and sessions petitioned Parliament to impose restrictions on spirit drinking, and, as a result, a series of Gin Acts were passed which diminished the evil to a certain extent.

INDUSTRIAL HYGIENE

The true father of industrial hygiene was Bernardino Ramazzini, Professor of Medicine in Modena University. About 1700 he published the result of his investigations in a work entitled *The Diseases of Artificers, which in their particular Callings they are most liable to, with the Method of avoiding them and their cure.* This was translated into English by Robert James, M.D., of *Fever Powders* fame in 1746.

The industrial changes in England during the latter half of this century mark the beginnings here of the study of the prevention of diseases of occupation. Medical practitioners could not help being concerned with the lowered physique, the increased amount of disease, the particular manifestations of disease, the higher mortality especially amongst women and children, and the malnutrition and crippling shown by persons employed in the new industries. In the eighteenth century the English

pioneers in this subject were Aiken, Thomas Percival and Ferriar, who formed with others a voluntary Board of Health to direct official and public attention to prevention of these evils.

A well-known example of industrial poisoning is Sir George Baker's investigation of lead colic derived from Devonshire cider. When lead was eliminated from the manufacturing process colic and palsies ceased.

JOHN HUNTER AND EDWARD JENNER

Our concern here is with the practitioners whose assembled work was advancing preventive medicine; and we have no leisure to dwell on the simultaneous advances made in medicine and surgery and in science generally. Yet we must pause for a moment to discern the form of a great surgeon, as Reynolds painted him, clad in red-purple velvet and pondering on the many problems that filled his inquiring mind. John Hunter, largely self-taught, devoted his life and much of his hardly-earned fees to comparative anatomy and experimental pathology and surgery. He elevated the empiricism of surgery into a science and his fame is eternal. His teaching influenced preventive medicine, and to his pupil, Edward Jenner, mankind owes the means of avoiding smallpox and the introduction of the practice of immunity.

The early years of the eighteenth century had seen the adoption of inoculation for the smallpox from Turkey, but this did not prevent the disease, as by cross-infection it increased its incidence, if not its mortality. Jenner did not discover vaccination, but he showed that cowpox was inoculable on man, could be transferred from man to man and that vaccinia protected man from smallpox. The ravages of smallpox prior to the introduction of vaccination were fearful. In London, alone, the Bills of Mortality continued to show to the end of the eighteenth century an average of 1,800 to 2,000 deaths from smallpox annually.

The eighteenth century marks a great advance in investigation and knowledge. The increase in medical epidemiology was already mainly responsible for a more rapid fall in the death-rate. "With all its faults the later Eighteenth Century was a period of improved science, cleanliness and humanity", writes Professor G. M. Trevelyan [6]. Later the laws of hygiene and social welfare were violated in the abrupt transition from rural to industrial England.

THE INFANCY OF STATE MEDICINE

It is apparent from our review of early Preventive Medicine that State Medicine was in its infancy when Queen Victoria ascended the throne in 1837. The reforming vision of Sir Thomas More in public health had long since departed from Councils of State, and the discoveries in the prevention of disease made in the eighteenth century were not as yet applied to national needs. Not that Governments ignored their responsibility for combating disease and preserving the health of His Majesty's subjects in times of dire necessity. As examples of such concern the edicts of Henry VIII and James I against plague and the steps taken by the City of London and the College of Physicians to combat the Great Plague may be cited. In 1720, Dr. Richard Mead in response to an appeal from the Secretary of State made under the threat of an attack of Levantine plague, which was spreading in the South of France, published his *Short Discourse Concerning Pestilential Contagion, and the Methods to be Used to Prevent It.* This not only advised what precautions might be taken for the public safety if plague spread to England, but advocated the setting up of a Council of Health entrusted with all requisite powers. The threatened danger passed and the Government of George I's day did not establish a Ministry of Health.

To take another instance, the Dissolution of the Monasteries, in spite of More's protests, involved the abolition of the hospitals maintained by the monks. Towards

William Smellie, a Scot, who had learned his midwifery in Paris, settled in London, and as practitioner, teacher and writer advanced knowledge of his subject. He elevated the status of the man-midwife; introduced forms of technique for the measurement of the pelvis, safe use of the forceps, diagnosis and treatment of *placenta prævia*, and improved modes of version. Another Scot, William Hunter, was primarily an anatomist, but he was also a practising obstetrician. His methods were conservative, but they were eminently sound. Hunter's pupil, Charles White of Manchester, in his excellent treatise, *On the Management of Pregnant and Lying-in Women and the means of curing but more especially of preventing the principal disorders to which they are liable*, published in 1773, dealt with the general management and hygiene of childbirth, ante-natal supervision, and the cause and prevention of puerperal fever. By his hygienic methods—scrupulous cleanliness, fresh air, suitable temperature of the lying-in ward, dietary and disinfection—he claimed that he had never lost a patient from puerperal fever. These three men, Smellie, Hunter and White, so greatly advanced obstetrics that further improvement was impracticable until Simpson discovered chloroform anæsthesia and Lister antiseptic surgery.

Side by side with improvement in maternal mortality can be noted the beginnings of infant welfare in isolated attempts to control the high mortality of infants and children, which amounted in 1730-49 to as much as 74% of children born. Lettsom and Cadogan especially drew attention to the subject, set up "infant dispensaries" and advised on the care of infants.

The Foundling Hospital, aimed at stopping the exposure, desertion and murder of infants, was established by Captain Thomas Coram in 1739. The financial difficulties of the hospital, the great demand for places and the terrible records of the deaths of children in the Bills of Mortality induced the Governors, of whom Jonas Hanway was one, to appeal to Parliament for help. From June 1756 to Ladyday 1760 the Hospital received all children brought to it, the cost being defrayed by a Treasury grant. After that it reverted to a private charity. Hanway also inspired the important Act of 1767 which boarded out parish children in London with carefully selected cottagers in the country. Howlett [13] estimated that the London burials were reduced by 2,240 in the first year and, that, allowing for the children who returned to London and died there, the annual average reduction in the London burials was 2,100.

Lettsom and others also advocated improved standards of nutrition for the population at large, and urged the restriction of or abolition of spirit drinking, which was then a cause of high mortality and a blot on our national civilization. The College of Physicians and numerous grand juries and sessions petitioned Parliament to impose restrictions on spirit drinking, and, as a result, a series of Gin Acts were passed which diminished the evil to a certain extent.

INDUSTRIAL HYGIENE

The true father of industrial hygiene was Bernardino Ramazzini, Professor of Medicine in Modena University. About 1700 he published the result of his investigations in a work entitled *The Diseases of Artificers, which in their particular Callings they are most liable to, with the Method of avoiding them and their cure.* This was translated into English by Robert James, M.D., of *Fever Powders* fame in 1746.

The industrial changes in England during the latter half of this century mark the beginnings here of the study of the prevention of diseases of occupation. Medical practitioners could not help being concerned with the lowered physique, the increased amount of disease, the particular manifestations of disease, the higher mortality especially amongst women and children, and the malnutrition and crippling shown by persons employed in the new industries. In the eighteenth century the English

pioneers in this subject were Aiken, Thomas Percival and Ferriar, who formed with others a voluntary Board of Health to direct official and public attention to prevention of these evils.

A well-known example of industrial poisoning is Sir George Baker's investigation of lead colic derived from Devonshire cider. When lead was eliminated from the manufacturing process colic and palsies ceased.

JOHN HUNTER AND EDWARD JENNER

Our concern here is with the practitioners whose assembled work was advancing preventive medicine; and we have no leisure to dwell on the simultaneous advances made in medicine and surgery and in science generally. Yet we must pause for a moment to discern the form of a great surgeon, as Reynolds painted him, clad in red-purple velvet and pondering on the many problems that filled his inquiring mind. John Hunter, largely self-taught, devoted his life and much of his hardly-earned fees to comparative anatomy and experimental pathology and surgery. He elevated the empiricism of surgery into a science and his fame is eternal. His teaching influenced preventive medicine, and to his pupil, Edward Jenner, mankind owes the means of avoiding smallpox and the introduction of the practice of immunity.

The early years of the eighteenth century had seen the adoption of inoculation for the smallpox from Turkey, but this did not prevent the disease, as by cross-infection it increased its incidence, if not its mortality. Jenner did not discover vaccination, but he showed that cowpox was inoculable on man, could be transferred from man to man and that vaccinia protected man from smallpox. The ravages of smallpox prior to the introduction of vaccination were fearful. In London, alone, the Bills of Mortality continued to show to the end of the eighteenth century an average of 1,800 to 2,000 deaths from smallpox annually.

The eighteenth century marks a great advance in investigation and knowledge. The increase in medical epidemiology was already mainly responsible for a more rapid fall in the death-rate. "With all its faults the later Eighteenth Century was a period of improved science, cleanliness and humanity", writes Professor G. M. Trevelyan [6]. Later the laws of hygiene and social welfare were violated in the abrupt transition from rural to industrial England.

THE INFANCY OF STATE MEDICINE

It is apparent from our review of early Preventive Medicine that State Medicine was in its infancy when Queen Victoria ascended the throne in 1837. The reforming vision of Sir Thomas More in public health had long since departed from Councils of State, and the discoveries in the prevention of disease made in the eighteenth century were not as yet applied to national needs. Not that Governments ignored their responsibility for combating disease and preserving the health of His Majesty's subjects in times of dire necessity. As examples of such concern the edicts of Henry VIII and James I against plague and the steps taken by the City of London and the College of Physicians to combat the Great Plague may be cited. In 1720, Dr. Richard Mead in response to an appeal from the Secretary of State made under the threat of an attack of Levantine plague, which was spreading in the South of France, published his *Short Discourse Concerning Pestilential Contagion, and the Methods to be Used to Prevent It.* This not only advised what precautions might be taken for the public safety if plague spread to England, but advocated the setting up of a Council of Health entrusted with all requisite powers. The threatened danger passed and the Government of George I's day did not establish a Ministry of Health.

To take another instance, the Dissolution of the Monasteries, in spite of More's protests, involved the abolition of the hospitals maintained by the monks. Towards

William Smellie, a Scot, who had learned his midwifery in Paris, settled in London, and as practitioner, teacher and writer advanced knowledge of his subject. He elevated the status of the man-midwife; introduced forms of technique for the measurement of the pelvis, safe use of the forceps, diagnosis and treatment of *placenta prævia*, and improved modes of version. Another Scot, William Hunter, was primarily an anatomist, but he was also a practising obstetrician. His methods were conservative, but they were eminently sound. Hunter's pupil, Charles White of Manchester, in his excellent treatise, *On the Management of Pregnant and Lying-in Women and the means of curing but more especially of preventing the principal disorders to which they are liable*, published in 1773, dealt with the general management and hygiene of childbirth, ante-natal supervision, and the cause and prevention of puerperal fever. By his hygienic methods—scrupulous cleanliness, fresh air, suitable temperature of the lying-in ward, dietary and disinfection—he claimed that he had never lost a patient from puerperal fever. These three men, Smellie, Hunter and White, so greatly advanced obstetrics that further improvement was impracticable until Simpson discovered chloroform anæsthesia and Lister antiseptic surgery.

Side by side with improvement in maternal mortality can be noted the beginnings of infant welfare in isolated attempts to control the high mortality of infants and children, which amounted in 1730-49 to as much as 74% of children born. Lettsom and Cadogan especially drew attention to the subject, set up "infant dispensaries" and advised on the care of infants.

The Foundling Hospital, aimed at stopping the exposure, desertion and murder of infants, was established by Captain Thomas Coram in 1739. The financial difficulties of the hospital, the great demand for places and the terrible records of the deaths of children in the Bills of Mortality induced the Governors, of whom Jonas Hanway was one, to appeal to Parliament for help. From June 1756 to Ladyday 1760 the Hospital received all children brought to it, the cost being defrayed by a Treasury grant. After that it reverted to a private charity. Hanway also inspired the important Act of 1767 which boarded out parish children in London with carefully selected cottagers in the country. Howlett [13] estimated that the London burials were reduced by 2,240 in the first year and, that, allowing for the children who returned to London and died there, the annual average reduction in the London burials was 2,100.

Lettsom and others also advocated improved standards of nutrition for the population at large, and urged the restriction of or abolition of spirit drinking, which was then a cause of high mortality and a blot on our national civilization. The College of Physicians and numerous grand juries and sessions petitioned Parliament to impose restrictions on spirit drinking, and, as a result, a series of Gin Acts were passed which diminished the evil to a certain extent.

INDUSTRIAL HYGIENE

The true father of industrial hygiene was Bernardino Ramazzini, Professor of Medicine in Modena University. About 1700 he published the result of his investigations in a work entitled *The Diseases of Artificers, which in their particular Callings they are most liable to, with the Method of avoiding them and their cure.* This was translated into English by Robert James, M.D., of *Fever Powders* fame in 1746.

The industrial changes in England during the latter half of this century mark the beginnings here of the study of the prevention of diseases of occupation. Medical practitioners could not help being concerned with the lowered physique, the increased amount of disease, the particular manifestations of disease, the higher mortality especially amongst women and children, and the malnutrition and crippling shown by persons employed in the new industries. In the eighteenth century the English

THE NEW HUMANITY AND THE SOCIAL REVOLUTION

It is recognized but insufficiently emphasized how material and general progress, as exemplified by new inventions and economic prosperity have increased the difficulties of public health reform. In the early part of the eighteenth century (1701-1759) England was an agricultural and pastoral country, which was producing a steadily decreasing surplus of grain, a surplus which was being exported and sold abroad. In this same century, as we have seen, there was an accumulating rise of new scientific knowledge as to the causes and preventabilities of different kinds of disease; and the country under the teaching of the "new humanity", whose prophets were the religious revivalists, John and Charles Wesley and George Whitefield and the practical philanthropists, Oglethorpe and John Howard, had advanced in the principles and practice of politics and sociology. Great Britain had, in fact, in the eighteenth century, begun a new national life with higher conceptions of political good, and preventive medicine would have had a much easier task in improving the health of a nation, which had continued to live chiefly in rural surroundings. The "new humanity" joined with the rising science of organized preventive medicine would have made giant strides in the improvement of national health had social and economic conditions remained as they were during the first half of the eighteenth century. There was, as has been said, a perceptible improvement. This is indicated by the fact that in the single reign of George III (1760-1820) the population of Great Britain rose from about seven and a half to fourteen millions. This unexampled rate was partly due to earlier marriages and an increase in the crude birth-rate, partly due to an improved standard of living, but mainly due to the more rapid fall in the death-rate which in turn depended on the increase in medical knowledge. Then came the discovery of steam and the harnessing of mechanical power to the service of man, which brought about the industrial revolution. This added greatly to the national wealth. To the superficial observer it was certainly progress to see the land, especially the north of England, studded with new factories employing a vast population of workers—men, women and children—to read of the large exports of iron, cotton and coal and to find Britain's merchant ships riding the seas in all four quarters of the globe. But from the aspect of national health it was not progress, because no attention was paid to the laws of hygiene and social welfare in the abrupt transition from rural to industrial England [9].

Towards the close of the eighteenth century the agricultural districts ceased to be adequate for the needs of the people and it became necessary to import wheat and other bread-stuffs. A much smaller acreage of land was under cultivation, because the tillers of the soil left the rural districts and flocked into the already congested towns. This process of migration was accentuated by an enforced migration from rural to urban centres due to the Enclosure Acts, which deprived the independent yeoman peasantry of their ancient rights as freeholders in order that large estates and farms might be increased. The intention was to augment the food supply of the country for the increasing population. In effect it depopulated the countryside; and, along with voluntary migration, it favoured overcrowding, disease and epidemics, and assisted to give England and Wales the problem of the slums, which only in comparatively recent times the State has been able to assail by its housing and overcrowding legislation.

Over and above all this, there were the terrible conditions of women and child slavery in the mines and factories. The horrors of the Factory System as it affected children are almost indescribable. The hours during which these unhappy helpless beings worked were excessive; they were harshly and sometimes cruelly treated; the time allowed for rest and meals was utterly insufficient; for education, moral and religious training and health no time at all was allowed. All day the iron wheels were droning and turning, grinding out the lives of little children, and the end of the seventeenth century Macaulay [7] states there was not then, in the whole realm, a single infirmary maintained by voluntary contribution. "Even in the capital the only edifices open to the wounded were the two ancient hospitals of Saint Thomas and Saint Bartholomew", preserved by the resolute action of the citizens of London in the sixteenth century. Yet after the naval Battle of La Hogue in 1692, fifty surgeons, plentifully supplied with instruments, bandages and drugs were sent down in all haste from London to Portsmouth at government expense, and Queen Mary, the wife of William III, gave orders that in the two London hospitals arrangements should be made at the public charge for the reception of patients from the Fleet, a precedent for the Emergency Hospital Service of the last war. The foundation of Greenwich Hospital for disabled seamen also dates from William and Mary's time. In the eighteenth century philanthropy caused many of the great London hospitals and a large number of provincial hospitals to be built, and there were certain workhouse infirmaries for the destitute poor.

The attitude of successive governments towards preventive medicine was much that of the ordinary man towards his private doctor. The government only sought medical advice from the Royal College of Physicians or individual leaders of the profession for the health of the community in cases of emergency, or when pestilence had appeared or was threatening. As Mead did, the advisers, in addition to necessary measures to deal with the immediate situation, not infrequently recommended some form of permanent state organization to maintain the public health, but the advice was ignored as soon as the emergency had passed.

The Fighting Services had displayed greater perspicacity. Sir John Pringle (1707-1782) by his work on *Diseases of the Army* had begun hygienic reform in the British Army, and Dr. James Lind and Sir Gilbert Blane were abolishing scurvy and advocating the study of hygiene in the Royal Navy.

The high incidence of disease and mortality in the civilian population for the most part went unheeded. Cholera appeared in the United Kingdom from 1831 to 1833, the first invaded port being Sunderland. A consultative Board of Health was set up under the Presidency of Sir Henry Halford, then President of the Royal College of Physicians, but its chief functions were restricted to the giving of medical advice as it had no executive authority. The advent of this new pestilence gave rise to an uneasy feeling that precautions taken after the introduction of disease instead of before the event were not altogether satisfactory.

Simon [8] sums up the situation in the following words:

> "Thus in 1830, when William the Fourth began his reign, and equally in 1837 when the reign ended, the new knowledge was virtually unrecognized by the Legislature. The Statute Book contained no general law of sanitary intention, except (so far as this deserves to be counted an exception) the Act providing for Quarantine, under which well-intentioned but futile Act, the Lords of the Council were supposed to be always on the look-out for transmarine dangers of pestilence, and could make pretence of resisting such dangers. Against smallpox, Parliament used annually to vote £2,000 to support a National Vaccine Board which had a few vaccinating stations in London, and furnished the public with vaccine lymph. Outside these two matters, the Central Government had nothing to say in regard to the Public Health, and Local Authorities had but the most indefinite relation to it. Various important towns had their special Improvement Acts for certain purposes: but among the purposes Health had hardly yet begun to stand on its own merits."

But now, in addition to the threat of pestilence, important social influences were in operation which were to break down the barriers hitherto interposed against national health reform. It will not be irrelevant to examine these influences and to see how they affected public opinion.

Jeremy Bentham (1748-1832) by his personality and doctrine, his breadth of view and prodigious range of knowledge left his mark alike on morals and legislation. "He had been in early life the friend of Adam Smith, the Wesleys, Mirabeau and William Pitt; later James Mill, Samuel Romilly, and Etienne Dumont were his comrades and disciples, while in the evening of his life Chadwick and Dr. Southwood Smith resided with him at his hermitage at Queen's Gate, Westminster, and acted as secretaries during the last three years of the octogenarian sage" [12].

Such were the influences at work which helped to constitute a powerful body of public opinion, forceful and articulate. By 1837 Parliament had instituted a number of substantial political reforms. Slavery had been abolished in the British colonies though not as yet in the factories and mines in England and Scotland; still, factory legislation had been initiated. The Roman Catholics had been emancipated; there was a new Poor Law, a certain amount of municipal reform had been effected; and the Registration of Births, Deaths and Marriages heralded the national vital statistics. Mechanical transport had come to complicate existence with steamboats, the steam engine and the beginnings of a railway system.

GRAVE IMPAIRMENT OF NATIONAL HEALTH

The Industrial Revolution, as we have seen, changed the character of England. Driven from their small-holdings by the Enclosure Acts, the peasants flocked to be employed in the new factories, and the towns in the industrial districts had to grow rapidly to accommodate them. This increased and sudden urbanization of the people in the late eighteenth and early nineteenth centuries created most serious sanitary problems. In the hasty building of the new industrial towns there was no idea of town planning and little thought for the future. The workers' environment was deplorable. In many cases the elementary rules of building construction were ignored in erecting houses. No attention was paid to suitability of soil, site, conveniences, curtilage, water supply and treatment of sewage. The houses were crowded together, built badly with indifferent materials, damp, badly lighted and ventilated, and often placed back to back. These houses being of small capacity the people inhabiting them were grossly overcrowded. Not only did the conditions in the mines and factories promote degradation, crippling and disease, but the home conditions of the workers were even worse. Dirt and disease, malnutrition and sometimes starvation prevailed, and these horrible conditions were aggravated by the increasing density of the population. In 1838 a joint report by Dr. Neil Arnott and Dr. James Phillips Kay and a report by Dr. Southwood Smith to the Poor Law Commissioners gave a terrible picture of the ravages inflicted by infectious disease in London at that time. They showed that out of 77,000 persons (in- and out-door paupers) 14,000 were attacked by fever, one-fifth part of the whole, and that out of the 14,000 attacked nearly 1,300 died. London provided the most glaring examples of this kind, but infectious diseases then rioted uncontrolled to a large extent throughout England. The chief diseases appear to have been typhus and typhoid fevers, cholera, smallpox, scarlet fever and measles.

To sum up, wretchedness, sickness and mortality prevailed among the working population. Infectious diseases wrought havoc among all classes of the community, for not infrequently fever was carried from the hovel to the mansion. The economic loss to the nation caused by ill-health must have been great.

CONCLUSION

It was now high time for the knowledge of hygiene and of the prevention of disease, already acquired by the medical profession, to be applied to the crying needs of the nation. The hour of deliverance had struck, and pioneers in both health and social reform were at hand. The work of Edwin Chadwick, Southwood squandering in the process the health and vitality of a considerable portion of the nation. As Dean Spence [10] wrote:

> "The poor little ones laboured like beasts of burden, and toiling on the long week through in their subterranean workshops, scarcely ever caught a sight of the sunshine during the six days of unremitting work. The seeds of many diseases were thus early sown. Many became permanently sickly, and not a few died."

Evil has many descendants and the appalling conditions which prevailed before reform came inevitably weakened healthy stocks and national stamina.

The reform came only by stages. In 1802 the first Sir Robert Peel, inspired by the medical findings of Percival and his associates, carried through Parliament his "merciful Act", which provided in some degree for care and education of these children. In 1819 he succeeded in obtaining another Act, which forbade children *under nine years of age* working in a cotton factory, while no young person under sixteen was to be allowed to work *more than twelve hours a day*, exclusive of meals. Further and more comprehensive legislation was attempted in 1830-31, but even then was sadly inadequate, until later legislation promoted by Lord Ashley, afterwards the seventh Earl of Shaftesbury, resulted in the Factory Acts.

With the Industrial Revolution, its benefits and its evils, came a sweeping change in the social hierarchy. The established authority of the landed classes was threatened by a rising middle class, rich in accumulated commercial wealth, and by the increasing population of workers—an urban population, which from the beginning of the nineteenth century grew at the rate of 30% every ten years. The workers agitated for lightening of taxation, bread at fixed price, reform of justice, universal suffrage and annual parliaments. The new commercial classes and the inhabitants of the rising towns demanded representation in Parliament and the abolition of the rotten boroughs. The Whigs adopted a policy of reform with a limited franchise and the artisans with a sound political instinct supported this as an instalment of more complete reform. In 1832 the Reform Bill was passed and opened a new era in English History. The will of the people had prevailed against a tradition of four hundred years of restriction and privilege.

As always happens in a revolutionary epoch, countless schemes were now mooted for the improvement of the human race and for the well-being of the British people in particular. They ranged from extreme views based on Thomas Paine's *Rights of Man* and communistic theories fathered by the Jacobins of the French Revolution to the Chartist movement which united radicals, socialists, trade unionists and the considerable women's suffrage clubs in a pledge to put aside all other questions until they had won the vote. These movements died away, but their very existence indicated that the mass of the people had deep-seated grievances to redress and could now unite to voice them [11].

In the new society which the Industrial Revolution had called into being the manufacturers and the workers demanded social reforms and were supported by scientists like Davy, Herschel, Watt and Stephenson; religious philanthropists, such as Zachary Macaulay, Clarkson, Wilberforce; and the secular reformers, James Mill, Romilly, Mackintosh, Huskisson, Jeremy Bentham and others. They ventilated such questions as universal suffrage, the ballot, reform of Parliament, freedom of the Press, just and equal laws and alteration of the savage and harsh penal code.

Of outstanding influence on the future of public health were the doctrines of the philosopher, Jeremy Bentham, who proclaimed that the end of all government must be utility, or the good of the governed. "The greatest happiness of the greatest number", as he phrased it, though the words were originally used by Joseph Priestley to produce anæsthesia adequate for dental extractions in a number of patients, although by ill-luck Wells's public demonstration was a failure.

In view of Wells's experience it is not at all surprising that Morton should have chosen sulphuric ether as his anæsthetic agent. Michael Faraday in 1818 had drawn attention to the similarity of the physiological effect produced by nitrous oxide gas and by ether vapour when inhaled, and in the eighteen-forties this similarity was widely recognized. Indeed Long had already chosen between these two agents.

During his preliminary trials of etherization Morton gleaned from the scientist C. T. Jackson (his former chemistry tutor) one very important hint—to use rectified ether, not that ordinarily sold. In devising an inhaler to be used at the demonstration arranged for October 16, Morton had the active help of another able Bostonian, the physician Augustus A. Gould. On the very eve of the demonstration this inhaler had not yet taken final shape, but after working with Gould far into the night, Morton next morning took the finished design to an instrument maker and remained supervising the making of the inhaler until the last possible moment. He arrived late in the operating theatre of the Massachusetts General Hospital with his inhaler untried.

John Collins Warren, the surgeon on that historic occasion, described how the patient (a young man from beneath whose jaw a tumour was to be removed) after inhaling for four or five minutes, appeared to be asleep. He remained so until the tying of the veins "during which", said Warren, "he began to move his limbs, cry out, and utter extraordinary expressions. These phenomena led to a doubt of the success of the application; and in truth I was not satisfied myself until I had, soon after the operation and on various other occasions, asked the question whether he had suffered pain. To this he always replied in the negative, adding, however, that he knew of the operation, and comparing the stroke of the knife to that of a blunt instrument passed roughly across his neck".

The apparatus which Morton had used consisted of a two-necked glass globe containing an ether-soaked sponge; in one neck was an inspiratory flap-valve, the other neck ended in a tube which the patient held in his lips (the outside of his mouth being cupped by a flange and his nostrils being pinched together by a bystander). Behind the mouth-tube was an expiratory valve, guarded by a metal cover. A fortuitous but important advantage lay in the fact that the administrator held this inhaler in his palm, and the natural warmth facilitated vaporization of the ether.

After Morton's demonstration various distinguished Bostonians who had witnessed it, hastened to send word of etherization to colleagues not only elsewhere in America but in Europe. Among the first to receive the news here was the American-born and educated Francis Boott, a physician living in Gower Street, London.

Boott immediately set about testing etherization for himself and, on December 19, 1846, he and a dentist named Robinson, after administering ether vapour to a certain Miss Lonsdale, extracted from her mouth "a firmly fixed molar tooth" without, as he said, "the least sense of pain, or the movement of a muscle. The whole process of inhalation, extracting and waking, was over in three minutes".

Boott also wrote to Robert Liston, Professor of Surgery in the University of London, and on Monday, December 21, Liston operated painlessly on two patients who inhaled ether from an apparatus improvised by Squire, of Oxford Street. One patient had his leg amputated at the thigh, the other had a toenail removed.

Squire's large, valved, sponge-filled glass inhaler was intended to stand by itself. A long, narrow tube led the ether-air mixture to a flanged mouth-tube, and the patient's nostrils were closed by a clip. This was the type of inhaler widely adopted both in the British Isles and on the European Continent during the early days of ether anæsthesia.

Smith, John Simon and Lord Shaftesbury created an administrative system of State Medicine which has achieved a position in the world second to none.

That golden story lies outside the purview of this Address. In the time at my disposal, I have tried to show you the beginnings of English Preventive Medicine, how physicians, surgeons and general practitioners—especially in the eighteenth century—sought painfully and carefully for the causes of disease and worked out measures of prevention. They worked alone for the most part. Many of them never saw the result of their labours. "Some there be which have no memorial."

But when philanthropists, humanitarians and administrators looked with sick and sorry hearts on the disease and many evils wrought by the Industrial Revolution, they turned to these enlightened members of the medical profession and found there was an answer to the social problems of the age. Thus English State Medicine was born. The administrators took the credit, often with justice, but the medical pioneers did the work, inspired appropriate legislation and made it practicable. That, however, is of little moment. Ours is characteristically a self-denying profession, and sees its reward in the conquest of disease, a greatly reduced mortality and the alleviation of pain and suffering.

Finis coronat opus.

REFERENCES

1 Herodotus (1894) Trans. by H. Cary, London. Euterpe II, 125.
2 MacNalty, A. S. (1946) (*a*) Sir Thomas More as Public Health Reformer, Chadwick Lecture; (1945) (*b*) The Renaissance and its Influence on Medicine, Surgery and Public Health. T. Vicary Lecture R.C.S., *Brit. med. J.* (ii), 755.
3 Osler, W. (1939) Aequanimitas, British Medicine in Greater Britain, 3rd Ed. London, 171.
4 Newman, G. (1932) The Rise of Preventive Medicine. London, 156.
5 Mackintosh, J. M. (1944) Preventive Medicine: Teaching and Practice, *Brit. med. J.* (ii), 53.
6 Trevelyan, G. M. (1929) History of England. London, 603.
7 Macaulay, T. B. (1871) History of England. London, 2, 358.
8 Simon, J. (1889) English Sanitary Institutions. London, Chap. 9, 166.
9 MacNalty, A. S. On the State of the Public Health, Ann. Rep. of the Chief Medical Officer of the Ministry of Health for the year 1938. London, H.M.S.O., 4.
10 Spence, H. D. M. (1898) The Church of England. London, 4, 396.
11 Green, J. R. (1921) A Short History of the English People, Epilogue by Alice Stopford Green. London, 852.
12 Collins, W. (1924) The Life and Doctrine of Sir Edwin Chadwick, published by the Chadwick Trust.
13 Howlett, J. (1781) Examination of Dr. Price's Essay on The Population of England and Wales. London, 91.
14 Manningham, R., (1744) An Abstract of Midwifery for the use of the Lying-in Infirmary; *see also* George, M. Dorothy (1930) London Life in the XVIIIth Century. London, Chap. 1, 48.

[*October* 16, 1946]

The Development of Inhalation Anæsthesia in the Second Half of the Nineteenth Century

By Barbara Duncum, Ph.D.

On this day one hundred years ago, William Thomas Green Morton, a dentist of Boston, in the United States of America, conclusively demonstrated what the Englishman, Henry Hill Hickman, had stoutly but unavailingly maintained during the eighteen-twenties, namely that surgical anæsthesia by inhalation was a practical proposition. That the time was now ripe for such a demonstration is shown by the fact that four years earlier, in 1842, and in the succeeding years, C. W. Long had performed minor operations painlessly on patients to whom he had administered the vapour of sulphuric ether. Morton was unaware of this, but he did know that his former partner, Horace Wells, had used nitrous oxide during the winter of 1844-5 to produce anæsthesia adequate for dental extractions in a number of patients, although by ill-luck Wells's public demonstration was a failure.

In view of Wells's experience it is not at all surprising that Morton should have chosen sulphuric ether as his anæsthetic agent. Michael Faraday in 1818 had drawn attention to the similarity of the physiological effect produced by nitrous oxide gas and by ether vapour when inhaled, and in the eighteen-forties this similarity was widely recognized. Indeed Long had already chosen between these two agents.

During his preliminary trials of etherization Morton gleaned from the scientist C. T. Jackson (his former chemistry tutor) one very important hint—to use rectified ether, not that ordinarily sold. In devising an inhaler to be used at the demonstration arranged for October 16, Morton had the active help of another able Bostonian, the physician Augustus A. Gould. On the very eve of the demonstration this inhaler had not yet taken final shape, but after working with Gould far into the night, Morton next morning took the finished design to an instrument maker and remained supervising the making of the inhaler until the last possible moment. He arrived late in the operating theatre of the Massachusetts General Hospital with his inhaler untried.

John Collins Warren, the surgeon on that historic occasion, described how the patient (a young man from beneath whose jaw a tumour was to be removed) after inhaling for four or five minutes, appeared to be asleep. He remained so until the tying of the veins "during which", said Warren, "he began to move his limbs, cry out, and utter extraordinary expressions. These phenomena led to a doubt of the success of the application; and in truth I was not satisfied myself until I had, soon after the operation and on various other occasions, asked the question whether he had suffered pain. To this he always replied in the negative, adding, however, that he knew of the operation, and comparing the stroke of the knife to that of a blunt instrument passed roughly across his neck".

The apparatus which Morton had used consisted of a two-necked glass globe containing an ether-soaked sponge; in one neck was an inspiratory flap-valve, the other neck ended in a tube which the patient held in his lips (the outside of his mouth being cupped by a flange and his nostrils being pinched together by a bystander). Behind the mouth-tube was an expiratory valve, guarded by a metal cover. A fortuitous but important advantage lay in the fact that the administrator held this inhaler in his palm, and the natural warmth facilitated vaporization of the ether.

After Morton's demonstration various distinguished Bostonians who had witnessed it, hastened to send word of etherization to colleagues not only elsewhere in America but in Europe. Among the first to receive the news here was the American-born and educated Francis Boott, a physician living in Gower Street, London.

Boott immediately set about testing etherization for himself and, on December 19, 1846, he and a dentist named Robinson, after administering ether vapour to a certain Miss Lonsdale, extracted from her mouth "a firmly fixed molar tooth" without, as he said, "the least sense of pain, or the movement of a muscle. The whole process of inhalation, extracting and waking, was over in three minutes".

Boott also wrote to Robert Liston, Professor of Surgery in the University of London, and on Monday, December 21, Liston operated painlessly on two patients who inhaled ether from an apparatus improvised by Squire, of Oxford Street. One patient had his leg amputated at the thigh, the other had a toenail removed.

Squire's large, valved, sponge-filled glass inhaler was intended to stand by itself. A long, narrow tube led the ether-air mixture to a flanged mouth-tube, and the patient's nostrils were closed by a clip. This was the type of inhaler widely adopted both in the British Isles and on the European Continent during the early days of ether anæsthesia.

News of surgical anæsthesia reached the Continent, and in particular France, at about the time that it reached Boott in England. Nevertheless it was not adopted there until the New Year. On January 21, 1847, the surgeon J. F. Malgaigne, at a meeting of the Académie de Médecine, in Paris, reported on five cases in which he himself had administered ether. Having no other kind of inhaler, Malgaigne introduced one end of a tube containing ether into his patient's nostril—the other nostril being plugged—and saw to it that inspiration took place through the nose, expiration through the mouth.

It was not only the surgeons who, during the early months of 1847, embarked on the further investigation of anæsthesia. Physiologists, also, carried out experiments with various potentially anæsthetic agents to ascertain individual properties and to establish their mode of action. Prominent in this field of research was the Frenchman, P. J. M. Flourens, who, during February and March 1847, experimented upon animals with sulphuric ether, ethyl chloride, and chloroform. He recorded that anæsthesia acted first upon the cerebrum—affecting the intellectual functions; secondly upon the cerebellum—deranging the equilibrium of movements; then upon the spinal cord—successively inhibiting sensibility and motility; finally upon the medulla oblongata—and when that phase was reached life became extinct.

In England, during February 1847, the physician John Snow also was carrying out experiments on animals. One conclusion he reached was that the anæsthetic agent acted by reducing oxidation in the body to a minimum. For the guidance of clinical administrators (of whom he was already one) Snow divided the progress of anæsthesia into five easily recognizable stages.

Anæsthesia in all its aspects was now Snow's dominant interest and henceforward he was acknowledged as the leading authority. He was quick to realize the shortcomings of inhalers such as Squire's. "When the inhalation of ether was first commenced", he wrote, "the inhalers employed consisted generally of glass vases containing sponge, to afford a surface for the evaporation of the ether. Both glass and sponge being very indifferent conductors of caloric, the interior of the inhalers became much reduced in temperature, the evaporation of ether was very much checked, and the patient breathed air much colder than the freezing point of water, and containing very little of the vapour of ether. On this account, and through other defects in the inhalers [elsewhere Snow mentioned faulty valves and tubing of too narrow bore], the patient was often very long in becoming insensible, and, in not a few cases, he did not become affected beyond a degree of excitement and inebriety."

Attempts to remedy these defects were indeed made early in 1847. Various kinds of valves were tried and inhalers were warmed by immersing them in hot water or by incorporating a warm-water chamber, but these empirical efforts were more often remarkable for ingenuity than for true insight into the problems of ether administration.

Snow was the first to design an inhaler based upon scientific reasoning. He worked upon the known fact that at different temperatures air will take up different amounts of ether vapour. When the inhaler was assembled for use, the metal carrying-case held water at a temperature of 50° F., and in this the ether vaporizing chamber was placed. The chamber contained a spiral baffle-plate to ensure that the air stream drawn in through a valveless tube by the patient came fully in contact with the liquid ether. Wide-bored, flexible tubing led the ether-air mixture to a valved facepiece—the latter an important innovation of Snow's, based upon a valveless facepiece devised by his friend Francis Sibson for anæsthetizing a patient with a facial tic. With the water-bath at 50° F., Snow's inhaler delivered an ether-air mixture containing 30% ether vapour. This mixture could be diluted by turning aside the expiratory flap-valve on the facepiece.

Despite the introduction of this inhaler, the difficulties which most people encountered in using ether made them anxious for some still more manageable means of anæsthetizing. This was supplied in November 1847, by James Young Simpson, Professor of Midwifery at Edinburgh. After testing a number of drugs, Simpson, at the suggestion of David Waldie, Chemist to the Apothecaries Company of Liverpool, tried chloroform. He found it, as he said, "infinitely more efficacious than any of the others", with the added advantage that "no special kind of inhaler or instrument is necessary for its exhibition. A little of the liquid diffused upon the interior of a hollow-shaped sponge, or a pocket-handkerchief, or a piece of linen or paper, and held over the mouth and nostrils, so as to be fully inhaled, generally suffices in about a minute or two to produce the desired effect".

Finding that this was indeed the case, medical men throughout the world immediately discarded ether and adopted chloroform.

Although it was not many weeks before deaths due to chloroform began to occur, such were the difficulties associated with etherization that only in the northern United States, in Lyons and through the Lyonnais example, in Naples, was a return made to its use. The reason for this return was, I think, because the Americans and the surgeons of Lyons had each hit upon a satisfactory method of administration. At the Massachusetts General Hospital, directly it became known that Morton was attempting to obtain a patent, the use of his inhaler was given up, and liquid ether was poured on to a bell-shaped sponge which was then firmly held over the patient's nose and mouth. The method of administering ether from a sponge, or from a sponge placed in the apex of a cone improvised from a folded towel, at once proved so simple and so satisfactory that it persisted in America, largely to the exclusion of other methods, until the end of the nineteenth century and after.

At Lyons, also, the method of etherization originally used there and re-adopted after the death of a patient under chloroform, was still in use in 1900. Liquid ether was poured into a bag, named after its inventor "Roux's *sac*". An air-port in the side could be opened or closed by a stopper. Strings drew the mouth of the bag snugly but not tightly round the patient's nose and mouth, and were then tied behind his head.

By about 1850, anæsthetic practice had assumed certain distinctive characteristics in different parts of the world. At Lyons and in the northern States of America ether was used, as I have just described. The southern States traditionally followed the example of Paris in medical matters; and in Paris chloroform was administered from a folded cloth, according to Simpson's directions. Not only the southern States of America, but the rest of France and indeed the rest of the Continent tended to copy Parisian methods. And in Scotland, of course, Simpson's method reigned supreme. In none of these places was it considered necessary to employ an expert anæsthetist and the task of administration was usually relegated to a junior house surgeon.

But in England a very different state of affairs obtained. Mainly, no doubt, because of John Snow's strong influence, the English almost from the first considered the giving of an anæsthetic to be a specialist's job, and believed that the use of some kind of regulating inhaler safeguarded the patient.

Simple and effective as Simpson's method of chloroform anæsthesia was, the English, by the beginning of 1848, had already devised a number of more or less elaborate chloroform inhalers, and Snow again controlled the anæsthetic mixture by regulating the temperature of the vaporizing chamber by a water-jacket. Snow's portable regulating chloroform inhaler served his contemporaries as a model until the introduction of Clover's chloroform apparatus in 1862. In the latter apparatus (which was itself based upon an experimental inhaler of Snow's) a mixture of 4½% chloroform

News of surgical anæsthesia reached the Continent, and in particular France, at about the time that it reached Boott in England. Nevertheless it was not adopted there until the New Year. On January 21, 1847, the surgeon J. F. Malgaigne, at a meeting of the Académie de Médecine, in Paris, reported on five cases in which he himself had administered ether. Having no other kind of inhaler, Malgaigne introduced one end of a tube containing ether into his patient's nostril—the other nostril being plugged—and saw to it that inspiration took place through the nose, expiration through the mouth.

It was not only the surgeons who, during the early months of 1847, embarked on the further investigation of anæsthesia. Physiologists, also, carried out experiments with various potentially anæsthetic agents to ascertain individual properties and to establish their mode of action. Prominent in this field of research was the Frenchman, P. J. M. Flourens, who, during February and March 1847, experimented upon animals with sulphuric ether, ethyl chloride, and chloroform. He recorded that anæsthesia acted first upon the cerebrum—affecting the intellectual functions; secondly upon the cerebellum—deranging the equilibrium of movements; then upon the spinal cord—successively inhibiting sensibility and motility; finally upon the medulla oblongata—and when that phase was reached life became extinct.

In England, during February 1847, the physician John Snow also was carrying out experiments on animals. One conclusion he reached was that the anæsthetic agent acted by reducing oxidation in the body to a minimum. For the guidance of clinical administrators (of whom he was already one) Snow divided the progress of anæsthesia into five easily recognizable stages.

Anæsthesia in all its aspects was now Snow's dominant interest and henceforward he was acknowledged as the leading authority. He was quick to realize the shortcomings of inhalers such as Squire's. "When the inhalation of ether was first commenced", he wrote, "the inhalers employed consisted generally of glass vases containing sponge, to afford a surface for the evaporation of the ether. Both glass and sponge being very indifferent conductors of caloric, the interior of the inhalers became much reduced in temperature, the evaporation of ether was very much checked, and the patient breathed air much colder than the freezing point of water, and containing very little of the vapour of ether. On this account, and through other defects in the inhalers [elsewhere Snow mentioned faulty valves and tubing of too narrow bore], the patient was often very long in becoming insensible, and, in not a few cases, he did not become affected beyond a degree of excitement and inebriety."

Attempts to remedy these defects were indeed made early in 1847. Various kinds of valves were tried and inhalers were warmed by immersing them in hot water or by incorporating a warm-water chamber, but these empirical efforts were more often remarkable for ingenuity than for true insight into the problems of ether administration.

Snow was the first to design an inhaler based upon scientific reasoning. He worked upon the known fact that at different temperatures air will take up different amounts of ether vapour. When the inhaler was assembled for use, the metal carrying-case held water at a temperature of 50° F., and in this the ether vaporizing chamber was placed. The chamber contained a spiral baffle-plate to ensure that the air stream drawn in through a valveless tube by the patient came fully in contact with the liquid ether. Wide-bored, flexible tubing led the ether-air mixture to a valved facepiece—the latter an important innovation of Snow's, based upon a valveless facepiece devised by his friend Francis Sibson for anæsthetizing a patient with a facial tic. With the water-bath at 50° F., Snow's inhaler delivered an ether-air mixture containing 30% ether vapour. This mixture could be diluted by turning aside the expiratory flap-valve on the facepiece.

Despite the introduction of this inhaler, the difficulties which most people encountered in using ether made them anxious for some still more manageable means of anæsthetizing. This was supplied in November 1847, by James Young Simpson, Professor of Midwifery at Edinburgh. After testing a number of drugs, Simpson, at the suggestion of David Waldie, Chemist to the Apothecaries Company of Liverpool, tried chloroform. He found it, as he said, "infinitely more efficacious than any of the others", with the added advantage that "no special kind of inhaler or instrument is necessary for its exhibition. A little of the liquid diffused upon the interior of a hollow-shaped sponge, or a pocket-handkerchief, or a piece of linen or paper, and held over the mouth and nostrils, so as to be fully inhaled, generally suffices in about a minute or two to produce the desired effect".

Finding that this was indeed the case, medical men throughout the world immediately discarded ether and adopted chloroform.

Although it was not many weeks before deaths due to chloroform began to occur, such were the difficulties associated with etherization that only in the northern United States, in Lyons and through the Lyonnais example, in Naples, was a return made to its use. The reason for this return was, I think, because the Americans and the surgeons of Lyons had each hit upon a satisfactory method of administration. At the Massachusetts General Hospital, directly it became known that Morton was attempting to obtain a patent, the use of his inhaler was given up, and liquid ether was poured on to a bell-shaped sponge which was then firmly held over the patient's nose and mouth. The method of administering ether from a sponge, or from a sponge placed in the apex of a cone improvised from a folded towel, at once proved so simple and so satisfactory that it persisted in America, largely to the exclusion of other methods, until the end of the nineteenth century and after.

At Lyons, also, the method of etherization originally used there and re-adopted after the death of a patient under chloroform, was still in use in 1900. Liquid ether was poured into a bag, named after its inventor "Roux's *sac*". An air-port in the side could be opened or closed by a stopper. Strings drew the mouth of the bag snugly but not tightly round the patient's nose and mouth, and were then tied behind his head.

By about 1850, anæsthetic practice had assumed certain distinctive characteristics in different parts of the world. At Lyons and in the northern States of America ether was used, as I have just described. The southern States traditionally followed the example of Paris in medical matters; and in Paris chloroform was administered from a folded cloth, according to Simpson's directions. Not only the southern States of America, but the rest of France and indeed the rest of the Continent tended to copy Parisian methods. And in Scotland, of course, Simpson's method reigned supreme. In none of these places was it considered necessary to employ an expert anæsthetist and the task of administration was usually relegated to a junior house surgeon.

But in England a very different state of affairs obtained. Mainly, no doubt, because of John Snow's strong influence, the English almost from the first considered the giving of an anæsthetic to be a specialist's job, and believed that the use of some kind of regulating inhaler safeguarded the patient.

Simple and effective as Simpson's method of chloroform anæsthesia was, the English, by the beginning of 1848, had already devised a number of more or less elaborate chloroform inhalers, and Snow again controlled the anæsthetic mixture by regulating the temperature of the vaporizing chamber by a water-jacket. Snow's portable regulating chloroform inhaler served his contemporaries as a model until the introduction of Clover's chloroform apparatus in 1862. In the latter apparatus (which was itself based upon an experimental inhaler of Snow's) a mixture of 4½% chloroform vapour in air was prepared and stored in a reservoir bag from which the patient inhaled it through a facepiece and tubing.

By 1864 the occurrence of deaths directly attributable to chloroform anæsthesia had become so formidable that a committee of investigation was appointed by the Royal Medical and Chirurgical Society. The majority of anæsthetists had long hoped for, and a few men, notably Snow, had actively sought some agent which would combine the convenience of chloroform anæsthesia with the avowedly greater safety of ether. It was by then evident that no such perfect anæsthetic would readily be found. So, chiefly through Joseph Thomas Clover (who, since Snow's death in 1858, had quietly become recognized as the new leader of the profession) the committee carried out a number of experiments with the two agents of proved worth—ether and chloroform. These experiments demonstrated anew that chloroform was the more dangerous because it acted directly upon the heart, whereas ether acted first upon the respiration, and in the event of an overdose the patient might be revived by artificial respiration. Despite these findings the committee, as it stated, concurred "in the general opinion which in this country has led to the disuse of ether as an inconvenient anæsthetic". To avoid the dilemma, the committee suggested that both agents should be used together in the hope that each might counteract the disadvantages of the other. The mixture particularly recommended was Harley's A.C.E., 1 part alcohol, 2 parts chloroform, 3 parts ether.

After the committee's report a new and more flexible attitude towards anæsthetic questions is perceptible in English practice, for it was at last beginning to be realized that no single agent could be expected completely to satisfy every requirement. This process of realization was hastened in 1868 by the introduction of nitrous oxide anæsthesia into English dental practice.

Nitrous oxide anæsthesia had been reintroduced into American dental practice in 1863, by G. Q. Colton, the itinerant, pseudo-scientific lecturer, whose demonstration of the properties of the gas at Hartford, Connecticut, in 1844, had been the cause of Wells's trial of its anæsthetic effect. During the International Exhibition in Paris, in 1867, Colton taught the American-born, Parisian dentist, T. W. Evans, to make and use the gas. In the following year, Evans made a special journey to London in order to pass on his knowledge to the chloroformists.

The Americans administered nitrous oxide either from a large rubber bag previously filled with it, or by letting the patient draw it directly from the generating apparatus through a mouthpiece and tubing. The English, led by Clover and by the dental surgeon, Alfred Coleman, were not slow in improving upon these methods. In the typical English apparatus, first put together in 1868 and retained in use during the next twenty-five years, the patient inhaled through a facepiece with a cushioned rim to ensure an airtight fit. (Colton had emphasized that the gas must be administered free from air.) Wide-bored tubing linked the facepiece to a reservoir bag, which had been added to the apparatus by W. A. N. Cattlin, a dentist. Narrow tubing connected with a cylinder of gas, which the firms of Barth and of Coxeter had succeeded in compressing on a commercial scale.

Although on the Continent the Franco-Prussian War seriously interfered with the adoption and development of nitrous oxide anæsthesia, an important contribution to its use was made by the French physiologist, Paul Bert. In 1878, Bert pointed out that so long as patients were forced to inhale undiluted nitrous oxide, anæsthesia would be complicated by asphyxia. He suggested that operations should be conducted in a chamber in which the pressure could be increased to two atmospheres. This would allow 50% of air or oxygen to be administered with the nitrous oxide. Bert's suggestion was adopted by a few surgeons, and for a year or two a mobile, positive pressure, operating theatre—Bert's anæsthetic car—plied between the hospitals of

Paris. In 1883, however, Bert proposed the simpler procedure of administering a mixture of oxygen and nitrous oxide at normal pressure. This procedure had already been put into practice in 1868, by Edmund Andrews, of Chicago. Curiously enough, neither Andrews's colleagues nor Bert's showed any great interest at the time; but indirectly through Bert's suggestion, nitrous oxide and oxygen anæsthesia was developed by the Russian obstetrician, Klikowitsch, and independently by various German and Austrian dentists—notably Hillischer of Vienna. It was through Hillischer's example that the English specialist anæsthetist, Frederic William Hewitt, during the last decade of the nineteenth century, was led to make very great improvements in the technique of nitrous oxide and oxygen anæsthesia.

In 1872, another American came to England bent on converting the chloroformists —this time to the use of ether. He was B. J. Jeffries, an ophthalmic surgeon from Boston, and the primary reason for his visit was an ophthalmological congress in London, at which he read a paper on the towel and sponge method of etherization. "Now if the patient is warned that ether will choke him", said Jeffries, "and told when this occurs to take long breaths to relieve it, and not struggle and endeavour to push away the sponge, many will go to sleep quietly and without trouble to themselves or the surgeon. . . . When the patient, whether old or young, struggles, and asks for a respite and fresh air, do not yield. Hold them down by main force if necessary, and, at any rate, keep the sponge tight over the mouth and nose till they finally take long breaths and then go off into ether sleep." Afterwards Jeffries gave demonstrations at several London hospitals, and though his uncompromising technique must have startled the cautious chloroformists, they readily admitted its success. By the spring of 1873 ether was once more in general use in this country, but already regulating inhalers were ousting the sponge and cone from use.

Of the various ether inhalers designed during the eighteen-seventies, two are outstanding—Ormsby's, and Clover's portable regulating inhaler. Both were described in the medical journals early in 1877. Clover himself, however, continued to prefer his apparatus for combined nitrous oxide and ether anæsthesia, on which he had begun to work as early as 1871, and which took its final form in 1876.

It seems probable that, as in the case of nitrous oxide anæsthesia, the troubled times following the Franco-Prussian War hindered the spread of the revived use of ether from England to the Continent. In 1877, in Geneva, however, the surgeon, Gustave Julliard, after a death from chloroform had occurred in his hands, abandoned the use of that anæsthetic and adopted etherization. He administered ether from a large face-mask, gauze lined but completely covered outside by waxed fabric impermeable to air. The use of this method gradually advanced northward and by 1890 had reached Tübingen in South Germany.

During the eighteen-eighties the surgeon Oscar Wanscher, of Copenhagen, also began to use ether—both rectally (a method originally introduced by the Russian surgeon Pirogoff, in 1847) and by inhalation. The inhaler which he used was a modification of Ormsby's. In 1890, the gynæcologist Landau, in Berlin, adopted Wanscher's method of inhaling ether. But in Germany as a whole, chloroform was exclusively used and was generally administered either from some variant of the small, open mask introduced into practice by Thomas Skinner, of Liverpool, in 1862, or from the inhaler originally designed by F. E. Junker in 1867, for administering B. W. Richardson's then new anæsthetic, bichloride of methylene. Junker, who was a Doctor of Medicine of Vienna, was at the time physician at the Samaritan Free Hospital in London.

The International Congress of Medicine in 1890 was held in Berlin, and the American pharmacologist, Horatio Wood, read a paper stressing, with statistical data, the relatively far greater safety of ether as compared with chloroform. The

Germans were impressed, and the surgeon, Ernst Gurlt, was commissioned independently to compile statistics relating to deaths under the two agents. Gurlt's figures, also, showed the superior safety of ether.

By 1894 many German surgeons were giving ether a re-trial—using either Julliard's mask or Wanscher's inhaler, and in the following year a few French surgeons (apart from those at Lyons) followed suit. But by the close of the century continental interest in etherization had begun to wane. For this, two main reasons can be found. One was the widely held belief that ether gave rise to post-operative chest complications; the other was the steadily growing interest in non-inhalation anæsthesia.

The adoption of anæsthesia in 1846 had made surgery more bearable for the patient, but his chances of survival were scarcely improved, because the occurrence of those septic conditions, known collectively as hospitalism, was increasing. However, after Lister's antiseptic method had been applied during and after the Franco-Prussian War, and when during the eighteen-eighties, the Germans replaced it by asepsis through heat sterilization, then at last visceral surgery could be and actually was undertaken with confidence, both in Germany and, through the German example, in the United States of America. In both countries the lack of expert anæsthetists was immediately felt. The surgeons looked with envy at the English specialist anæsthetist, but the urgency of the problem led them, during the eighteen-nineties, to find their own solution. They themselves prepared a painless operating field, at first by Schleich's local infiltration, later by regional nerve blocking and by spinal analgesia.

In Great Britain these new methods were looked at askance, although at the time of the jubilee of ether anæsthesia in 1896, and of chloroform in the following year, English anæsthetic practice itself had come under the critical scrutiny of men such as Hewitt and D. W. Buxton. Reluctantly they reached the conclusion that, compared with the enormous initial advances of 1846-7, subsequent progress had been in some ways disappointing. In particular they deplored the fact that the ordinary medical student—the potential occasional anæsthetist—still did not receive any adequate teaching in anæsthetics. The specialist anæsthetist, on the other hand, might well congratulate himself on his mastery of the techniques of nitrous oxide, of ether, and of chloroform anæsthesia—to which last agent the Hyderabad Chloroform Commissions of 1888 and 1889 had redirected attention—and there could be no doubt that in the field of inhalation anæsthesia he still excelled.

Section of Psychiatry

President—Professor Aubrey Lewis, M.D.

[*November* 12, 1946.

The Measurement of Personality. [*Résumé*]

By H. J. Eysenck, Ph.D.London
Psychological Laboratory, The Maudsley Hospital

Both terms in the title of this paper, "measurement" and "personality" need, definition and discussion, as common usage of these words is rather indeterminate. Personality we shall define, following Warren (1934), as "the integrated organization of all the cognitive, affective, conative, and physical characteristics of the individual as it manifests itself in focal distinctness to others." This rather inclusive definition distinguishes "personality" from such more narrowly circumscribed terms as "temperament" and "character," which refer more specifically to the affective and conative organization of the individual respectively, from "intelligence," which refers to the cognitive aspects, and from "constitution," which refers to the physical aspects.

If we accept this definition, it becomes clear at once that we cannot in any intelligible fashion talk about the *measurement* of personality. Without going into a detailed discussion of the principles of measurement (Campbell, 1928, 1938; Scates, 1937; Thomas, 1942; Young and Householder, 1941; Gulliksen, 1946), it is apparent that measurement can only proceed along one dimension at a time; we can measure the height of a building, or its length, or its depth—we cannot measure all three at the same time.

This difficulty lies at the back of Henderson and Gillespie's (1943) statement that "if it is doubtful what we measure with 'intelligence' tests, it is still more uncertain what we would try to measure if we tackled 'emotions' in a similar way". In other words, while in the cognitive sphere we have succeeded to some extent in isolating one "dimension" of personality for measurement, there is still no agreement about the "dimensions" existing in the orectic sphere, and consequently the very basis for any kind of measurement is absent.

Under those conditions, it behoves us to study the methods used in establishing the cognitive dimension, and to inquire whether the same methods might not with advantage be applied to the orectic sphere as well. Two main contributions may be discerned in the development of the science of intelligence measurement: one, the creation of a large number of objective, reliable tests validated against external criteria, such as judgments by teachers, parents, officers, psychiatrists, and so forth; and second, the elaboration of statistical methods, more particularly the method of factor analysis (Burt, 1940; Thomson, 1939; Guilford, 1937; Thurstone, 1935; Spearman, 1927), which ensure unidimensionality and internal validity to these tests.

In noting these two contributions, we find that both claim "validity" of testing as part of their achievement. This indicates that there are two different types of "validity". Validity is usually defined as a measure of the extent to which a test agrees with a criterion; e.g. the extent to which an intelligence test succeeds in measuring intelligence. But the example itself shows immediately that this definition is almost valueless; how *can* we know how well a test measures a quality, such as intelligence, unless we already have a perfect measure of that quality? True, we have a number of obviously imperfect measures of intelligence, such as teachers' ratings, success in school and college, or earning capacity, but as these criteria themselves are unequal, the question arises, which are we to choose? What criterion shall we use for choosing our criterion? In this way we become involved in an infinite regression, and our definition, so simple and obvious at first glance, is seen to be swallowed up by a metaphysical hydra.

As opposed to this "external" type of validity, psychologists have elaborated an "internal" validity, derived from the pattern of interrelations obtaining among groups of tests. Thus, fifty tests presumed to measure a great variety of aspects of intellectual ability are given to large numbers of subjects, the intercorrelations of the tests are calculated, and from the pattern or matrix of their intercorrelations certain "factors" are extracted whose validity does not depend on any outside criterion, but is derived from the whole "gestalt" of the original matrix. In this way, Spearman originally proved that there is one general factor, "g", which is common to all cognitive tests, in various proportions; in this way, we have learned since that there are a number of more specialized groups of abilities, common to some but not all tests, called verbal, arithmetical, visuo-spatial, æsthetic, mechanical and perceptual ability.

Superficially, the fact that we have two kinds of validity seems to face us with an impasse. The "intelligence" measured by the common-sense type of person who relies on external validity is not acceptable to the statistically minded psychologist, who is apt to raise awkward questions about the external criterion and its validity; the "g" measured by the statistical psychologist is said (by the non-statistician) to be a mere statistical artefact, without any real psychological meaning. Fortunately, there is a strong tendency for both types of validation to give the same answer to the question—which is the best test of intelligence? When we compare the correlations of a number of tests with an external criterion, we see that some tests correlate highly, others show low correlations. When we intercorrelate these same tests, and factor-analyse the resulting matrix, we find that some tests have high correlations with the resulting "g" factor, while others have low correlations. Now in such a situation it is usually found that the test that correlates highly with the outside criterion will also be the test that has a high factor saturation, and the test that shows a low correlation with the outside criterion also has a low factor saturation. In that way, we can identify our statistical factor, "g", with the psychological dimension, intelligence, and justly claim that we have succeeded in identifying and measuring this particular aspect of personality.

These considerations suggested that a similar process in the orectic field might lead to similar results; in other words, it appeared that the use of factorial analysis in connexion with temperament, character, and constitution might lead to the isolation, and finally to the measurement, of the main dimensions in those fields. Working on that basis, a team of psychologists and psychiatrists spent some four years at Mill Hill Emergency Hospital, and at the Maudsley Hospital, carrying out large-scale factorial and experimental studies into those problems; preliminary results have been published in a series of papers (*see* References: Eysenck, with Furneaux, Halstead. Himmelweit, Rees, and Yap). More recently, a complete account of this work has been published in book form (Eysenck, 1946). Only the main conclusions can be presented here.

Using factorial techniques as "internal validity" criteria, and psychiatric judgments, personal history data. Service career, and similar data as "external validity" criteria, we found that just as there is one general factor dominant in the cognitive field, so there are discernible strong general factors in the fields of character.and temperament as well, using our definitions of these terms as presented in the first paragraph of this paper.

In the field of character, or "conation", there appeared a very powerful factor which might be called neuroticism, maladjustment, neurotic constitution, lack of integration, or lack of will-power; this factor clearly distinguished (1) the person referred to a neuropsychiatric hospital from the person not so referred; (2) the neurotic patient judged by the psychiatrist to be severely ill from the patient judged to be less severely ill; (3) the "normal" person outside the hospital whose adjustment to Army, factory, or life was considered faulty from the person whose adjustment was more successful.

These findings were checked and counterchecked using a great variety of objective, reliable tests. The most successful of these tests was the "body sway" test of primary suggestibility, which was described in a paper read to this Society two years ago (Eysenck, 1943*a*). Another successful test was an objective version of the Rorschach ink-blot test, in which the subject has to select responses from a printed list, instead of providing original responses. A third type of test which gave adequate differentiation was a test of persistence, requiring the subject to maintain a certain posture involving fatigue of various muscles for as long as possible. Questionnaires, although less objective than the other tests in our battery, tended to give excellent results when given to suitable groups.

Other differences between persons situated towards the "neurotic" end of the dimension under discussion, and persons situated towards the "normal" end included the following: neurotics tended to be slightly less intelligent, although the difference was too small to be of any practical importance; they tended to have a markedly more leptomorphic body-build; they tended to score very badly on tests of dark-vision; they had a slow "personal tempo", low fluency, extreme perseveration (as opposed to lack in persistence) poor effort response, and a very uneven and irregular work-curve. On all these points, as well as on many others, there was good correspondence between external and internal criteria.

Whenever attempts were made to investigate the distribution of this factor, we found a roughly normal curve of distribution; this would appear to indicate that this factor may have a constitutional basis, and may be subject to multifactorial inheritance, like intelligence. Investigation of this possibility is urgently needed before any definite claims can be made as to the genotypical reality of our findings; factor analysis cannot give any but descriptive, phenotypical results, the possible causation of which must be investigated by other methods more directly concerned with the specific problem under discussion.

It is possible that the use of the term "neuroticism" in denoting this factor may be open to criticism, and indeed the multiplicity of meanings associated with

Under those conditions, it behoves us to study the methods used in establishing the cognitive dimension, and to inquire whether the same methods might not with advantage be applied to the orectic sphere as well. Two main contributions may be discerned in the development of the science of intelligence measurement: one, the creation of a large number of objective, reliable tests validated against external criteria, such as judgments by teachers, parents, officers, psychiatrists, and so forth; and second, the elaboration of statistical methods, more particularly the method of factor analysis (Burt, 1940; Thomson, 1939; Guilford, 1937; Thurstone, 1935; Spearman, 1927), which ensure unidimensionality and internal validity to these tests.

In noting these two contributions, we find that both claim "validity" of testing as part of their achievement. This indicates that there are two different types of "validity". Validity is usually defined as a measure of the extent to which a test agrees with a criterion; e.g. the extent to which an intelligence test succeeds in measuring intelligence. But the example itself shows immediately that this definition is almost valueless; how *can* we know how well a test measures a quality, such as intelligence, unless we already have a perfect measure of that quality? True, we have a number of obviously imperfect measures of intelligence, such as teachers' ratings, success in school and college, or earning capacity, but as these criteria themselves are unequal, the question arises, which are we to choose? What criterion shall we use for choosing our criterion? In this way we become involved in an infinite regression, and our definition, so simple and obvious at first glance, is seen to be swallowed up by a metaphysical hydra.

As opposed to this "external" type of validity, psychologists have elaborated an "internal" validity, derived from the pattern of interrelations obtaining among groups of tests. Thus, fifty tests presumed to measure a great variety of aspects of intellectual ability are given to large numbers of subjects, the intercorrelations of the tests are calculated, and from the pattern or matrix of their intercorrelations certain "factors" are extracted whose validity does not depend on any outside criterion, but is derived from the whole "gestalt" of the original matrix. In this way, Spearman originally proved that there is one general factor, "g", which is common to all cognitive tests, in various proportions; in this way, we have learned since that there are a number of more specialized groups of abilities, common to some but not all tests, called verbal, arithmetical, visuo-spatial, æsthetic, mechanical and perceptual ability.

Superficially, the fact that we have two kinds of validity seems to face us with an impasse. The "intelligence" measured by the common-sense type of person who relies on external validity is not acceptable to the statistically minded psychologist, who is apt to raise awkward questions about the external criterion and its validity; the "g" measured by the statistical psychologist is said (by the non-statistician) to be a mere statistical artefact, without any real psychological meaning. Fortunately, there is a strong tendency for both types of validation to give the same answer to the question—which is the best test of intelligence? When we compare the correlations of a number of tests with an external criterion, we see that some tests correlate highly, others show low correlations. When we intercorrelate these same tests, and factor-analyse the resulting matrix, we find that some tests have high correlations with the resulting "g" factor, while others have low correlations. Now in such a situation it is usually found that the test that correlates highly with the outside criterion will also be the test that has a high factor saturation, and the test that shows a low correlation with the outside criterion also has a low factor saturation. In that way, we can identify our statistical factor, "g", with the psychological dimension, intelligence, and justly claim that we have succeeded in identifying and measuring this particular aspect of personality.

These considerations suggested that a similar process in the orectic field might lead to similar results; in other words, it appeared that the use of factorial analysis thymes, while our extraverts (hysterics) tended to be eurymorphic in body-build. But in Kretschmer's system, hysteria tends to go with the schizothyme type, and depression with the cyclothyme type; consequently it does not appear that any identification of these two systems is possible. On colour-form tests, on which great differences usually become apparent between cyclothymes and schizothymes—the former being more colour-reactive, the latter more form-reactive—and on the reversal-of-perspective tests, in which also great differences usually appear—the cyclothymes giving fewer reversals than the schizothymes—no differences appeared between our extravert and introvert samples.

Our findings, while largely based on various neurotic groups, are also applicable, in our view, to normal groups; whenever we have had an opportunity of testing normal samples of the population we have found precisely the same differentiation in our test results as we found in our neurotic groups. As the total number of cases studied is quite considerable, approaching twenty thousand, we believe that our conclusions, while no doubt subject to many detailed criticisms and improvements, are perhaps a useful first approximation to the goal we set ourselves, viz. the isolation and measurement of the major dimensions of personality. This hope is strengthened by the fact that whenever it was found possible to check certain partial findings against the results obtained by other workers in the field, using quite different types of subjects (students, children, factory workers, &c.), considerable agreement was evident. Similarly, our main conclusions on the factorial side are not in contradiction to the results obtained in certain pioneer studies by Burt, Webb and others. A full discussion of the relation of our work to that of others will be found in "Dimensions of Personality" (Eysenck, 1947).

The picture of personality which emerges from these studies bears some similarity to a globe, or sphere. Any point on that sphere can be identified by reference to three axes constructed at right angles to each other, and penetrating the sphere. One of these axes is the familiar cognitive axis, labelled "g" or intelligence; the second axis is labelled "neuroticism", and may be identified with the conative side of personality; the third axis is labelled "introversion-extraversion", and corresponds to the affective side of personality. In actual fact, these three axes are not quite orthogonal, but show a slight degree of obliqueness; in other words, the angles separating them are not right angles, but only approach this particular structure. For instance, intelligence and neuroticism show a negative correlation of –0·30, corresponding to an angle deviating by 3 degrees from a right angle. A similar correlation is found between introversion and intelligence, again slightly tilting the two axes towards each other. But by and large these departures from orthogonality are too small to influence the general picture to any significant extent, and for practical purposes we may assume independence among our dimensions.

If we want to extend our personality sphere still further, so as to take in the physical aspect as well, we must add a fourth axis, at right angles to the other three; this addition of course necessitates a four-dimensional representation, and makes it impossible to visualize the resulting structure. Again slight departures from orthogonality must be admitted; leptomorph body-build correlating to the extent of 0·30 approximately with "neuroticism", and to the same extent with "introversion". It is not possible to say whether such a four-dimensional picture is adequate, or whether other dimensions will be required; only further research can answer this question.

The main usefulness of these studies, assuming that our general conclusions be accepted, will probably lie in two fields. In the first place, practical work in industrial psychology, vocational guidance, occupational selection, in clinical psychology, and in educational psychology, may benefit from the possibility of carrying out objective psychiatric terms such as ''neurosis'' makes them of doubtful value if applied to more specific findings with operational connotations. However, no other term could be found to obviate these difficulties, and in any case problems of nomenclature are of semantic rather than of scientific interest.

In the field of temperament, or ''affection'', there appeared a factor which seemed to be very similar in nature to Jung's extravert-introvert dichotomy. Among the neurotic patients investigated, this distinction pointed to a dimension ranging from one extreme, containing the more hysterical types of symptoms and reactions, to the other extreme, containing anxiety, depression, obsessional and other ''dysthymic'' reactions. These two groups of symptoms, the hysteric and the ''psychasthenic'' or, as we prefer to call it, the affective or dysthymic, are of course the prototypes of Jung's famous dichotomy, and thus our results strongly support his claims. It should be noted, however, that we regard extraversion and introversion not as types in the sense that a given person is either an extravert or an introvert; we merely regard these two concepts as the extreme ends of a normal curve of distribution, with the majority of people falling somewhere in between the extremes. Support for this view of a normal distribution of this factor comes from actually plotted distributions, all of which resemble the normal curve so familiar from work on intelligence tests.

Experimental measurement along this dimension is based on a variety of findings, involving a number of tests from various modalities. To begin with, there is strong evidence that the introverts tend to be leptomorphic in body-build, while the extraverts tend to be eurymorphic. Jones and Richter have shown that effort response is poorer in the introverts, and choline esterase secretion more pronounced. Intellectually, the introverts tend to score more highly; when equated for intelligence, introverts tend to give markedly higher scores on vocabulary tests than do extraverts. Introverts tend to carry out various tasks slowly, but accurately; extraverts tend to do them quickly and inaccurately. Introverts tend to have a high level of aspiration, to be very rigid in their demands of themselves, and to underrate their own performances; extraverts tend to have very low levels of aspiration, to lack the rigidity of the introvert, and overrate their own performances. These tendencies are exaggerated in the neurotic extravert (i.e. the hysteric) and in the neurotic introvert (i.e. the dysthymic); normal subjects are intermediate between these extremes.

Extraverts also tend to be differentiated from introverts by their æsthetic preferences, in terms of their sense of humour (both with respect to how amusing they find various types of material, and which type of material they find most amusing; on the whole, introverts find all types of material less amusing than do extraverts, but in the field of sexual humour in particular this difference is much more pronounced than elsewhere), and in terms of their æsthetic creativity, as shown for instance in the Lowenfeld Mosaic Test, where introverts tend to make compact, extraverts scattered designs. Questionnaires also show marked differences between introverts and extraverts, as do various other tests not enumerated.

It is important to clarify the relation of our introvert-extravert factor to Kretschmer's cyclothyme-schizothyme typology. It is our considered opinion, based upon a variety of experimental evidence, that these two typologies cannot justifiably be considered identical, and that in reality there is no relation between them whatsoever. In terms of experimental work, this conclusion follows from our demonstration that tests which had been shown by others to differentiate between cyclothymes and schizothymes did not discriminate at all between extraverts and introverts. The tests used included a variety of colour-form tests, reversal-of-perspective tests, and measurements of body-build. As already explained, we found that introverts (dysthymics, i.e. persons suffering from anxiety and reactive depression) tended to be leptomorphic in body-build, which would align them with Kretschmer's schizo-

Section of Neurology

President—DOUGLAS MCALPINE, M.D., F.R.C.P.

[*November* 7, 1946]

MEETING AT THE MAIDA VALE HOSPITAL FOR NERVOUS DISEASES, W.9.

Ataxic Nystagmus in Disseminated Sclerosis.—WILFRED HARRIS, M.D., F.R.C.P.

A man aged 39, began to be tremulous and unsteady three years ago, with weakness especially of the left arm and leg. He is now a typical case of disseminated sclerosis, is so unsteady that he cannot walk alone without a stick and someone to assist him. Typical inco-ordination of the arms, and some bladder weakness. Deep reflexes much increased. He shows two forms of nystagmus:

(1) Jelly nystagmus, a quivering motion of the eyeballs, which can only be seen by direct ophthalmoscopy, and

(2) Ataxic nystagmus. This latter form I described in *Brit. J. Ophthal.*, 1944, 28, 40. Briefly it consists of nystagmus of the outer eye only, the inner eye not quite reaching the canthus in conjugate lateral movement. This peculiar one-sided nystagmus of the outer eye may be seen both on looking to right and to left, or it may be to one side only. In this patient it is more marked on looking to the right, the right eye then showing coarse nystagmus with quick outward movement and slow return, the left eye remaining stationary and not quite reaching the inner canthus. I have seen a large number of similar cases in the last twenty years since I first noticed this type, and I consider it to be pathognomonic of disseminated sclerosis, as it does not occur in any other condition. It is obviously associated with weakness of the lateral conjugate movement of the eyes.

Jelly nystagmus was considered by Kinnier Wilson, 1940, "Neurology", 1, 161, London, quoting Paton, to be pathognomonic of disseminated sclerosis, but this form has been met with in other conditions.

Dr. Harris then showed a film produced by the Gaumont-British Co. of the patient walking; it also illustrated the inco-ordination of the arms. A close-up showed well the ataxic nystagmus.

The President said that the film was most interesting. It was probable that they had all seen this type of nystagmus, but had not realized its significance in relation to disseminated sclerosis.

Tuberose Sclerosis with Intracranial Calcification and Lesions of Bone.—HELEN DIMSDALE, M.R.C.P.

L. S., female, aged 39.

Family history.—8 normal siblings. Father dead—"consumption" and alcoholism. Mother aged 83, alive and well. No family history of fits or mental deficiency.

History.—Development normal till age of 5 when she started to have fits and a rash was noticed on her face. Dull at school, but learned to read and write. Earned her living as a domestic worker. Incidence of fits variable and unaffected by sedatives.

On examination.—Facial adenoma sebaceum of Pringle type, scattered cutaneous and subcutaneous fibromata, large shagreen patch in lumbosacral region. Adherent lobes to ears. C.N.S.: High-grade mental defective. Fundi: no lesions detected. No focal signs.

Investigations.—C.S.F.: Normal pressure and constituents. Blood W.R. negative. Serum calcium: 10·3 mg.%. Inorganic phosphorus: 3·4 mg.%. Serum phosphatase: 3·0 units. X-rays: Chest: N.A.D. Skull: Hyperostosis frontalis interna. Choroid plexuses heavily calcified. Two patches of paraventricular calcification. Hands and feet: Periosteal thickening metacarpals and metatarsals, areas of rarefaction in terminal phalanges suggestive of small cysts. Spine: vestigial twelfth ribs; no evidence of spina bifida.

measurement along the two dimensions indicated. In the second place, the provision of batteries of tests for such measurement will make possible a concentrated attack on such theoretical problems of outstanding importance as the influence of nature and nurture in the genesis of conative and affective traits, or the relation of personality variables to a great variety of psychological phenomena. Only by such further experimentation can the claims made here be proved or refuted, and our knowledge in the field of personality measurement be extended beyond the present narrow boundaries which have prevented its growth for too long.

REFERENCES

BURT, C. (1940) The Factors of the Mind. London.
CAMPBELL, N. R. (1928) An Account of the Principles of Measurement and Calculation. London.
—— , (1938) Symposium: Measurement and Its Importance for Philosophy, *Proc. Arist. Soc. Suppl.*, London, 17, 121.
EYSENCK, H. J. (1943*a*) *Proc. R. Soc. Med.*, 36, 349.
—— (1943*b*) *Lancet*, (ii), 362.
—— (1943*c*) *J. Neurol. Psychiat.*, 6, 22.
—— (1944*a*), *Brit. J. med. Psychol.*, 20, 100.
—— (1944*b*) *Amer. J. Psychol.*, 57, 406.
—— (1944*c*) *J. ment. Sci.*, 90, 851.
—— (1945*a*) *Brit. J. Psychol.*, 35, 70.
—— (1945*b*) *Psychol. Bull.*, 42, 659.
—— (1947) Dimensions of Personality. London.
——, and FURNEAUX, W. D. (1945) *J. exp. Psychol.*, 35, 485.
——, and HALSTEAD, H. (1945) *Amer. J. Psychiat.*, 102, 174.
——, and HIMMELWEIT, H. T. (1946) *J. gen. Psychol.*, 35, 59.
——, and REES, W. L. (1945) *J. ment. Sci.*, 91, 301.
——, and YAP, P. M. (1944) *J. ment. Sci.*, 90, 595.
GUILFORD, J. P. (1937) Psychometric Methods. New York.
GULLIKSEN, H. (1946) *Psychol. Rev.*, 35, 199.
HENDERSON, D. K., and GILLESPIE, R. D. (1943) A Text Book of Psychiatry. Oxford.
HIMMELWEIT, H. T. (1946) *Brit. J. Psychol.*, 36, 132.
—— (1945) *J. Person.*, 14, 93.
REES, W. L. (1945*a*) *J. Neurol., Neurosurg., Psychiat.*, 8, 34.
——, and EYSENCK, H. J. (1945*b*) *J. ment. Sci.*, 91, 8.
SCATES, D. E. (1937) *Psychometrika*, 2, 27.
SPEARMAN, C. (1927) Abilities of Man. London.
THOMAS, L. G. (1942) *Psychol. Monogr.*, 54, No. 3.
THOMSON, G. H. (1939) The Factorial Analysis of Human Ability. London.
THURSTONE, L. L. (1935) Vectors of Mind. Chicago.
WARREN, H. C. (1934) Dictionary of Psychology. Boston.
YOUNG, G., and HOUSEHOLDER, A. S. (1938) *Psychometrika*, 3, 19.
——, —— (1941) *Psychometrika*, 6, 331.

is sufficient to remove an inch or so of the styloid process and there is no need to do anything more to the nerve.

I agree with Dr. McAlpine that the type of case which appears to be suitable for this operation is one in which there is no evidence of any primary condition which is apparently causing the neuralgia and a trigger area should be present in the tonsillar region; if these two conditions apply the operation should prove a very successful one.

Dr. Wilfred Harris: Glossopharyngeal neuralgia is rare compared to trigeminal tic, perhaps in the ratio of 1 : 500. A characteristic sign sometimes met with is a hawking cough in the effort to arrest the pain. Avulsion of the nerve after dissection behind the angle of the jaw has proved very satisfactory in many cases, though it may prove a difficult operation. It has the advantage that steady traction may bring away with it both the jugular and petrous ganglia. Mr. Wilson's method may prove easier to those accustomed to work inside the mouth.

Dr. C. Worster-Drought said that he thought the very satisfactory result of the operative treatment in this case depended on the situation of the "trigger zone". In other cases of glossopharyngeal neuralgia and without such a "trigger zone" the result might not be so successful. In the cases he had seen, complete avulsion of the nerve through an incision in the upper part of the neck had usually resulted in complete relief. The portion of the nerve removed, however, must include both the ganglia, viz. the jugular ganglion and the petrous ganglion. In one case in which the ninth nerve was divided between the two ganglia the pain was not relieved.

Mr. G. C. Knight: I would like to congratulate Mr. Wilson upon devising such an excellent and simple method of treatment of glossopharyngeal neuralgia. There can be no doubt that the operation formerly employed of deep dissection of the neck to secure a division of the glossopharyngeal nerve at the base of the skull could be a most difficult procedure in a thick-necked individual, for the glossopharyngeal nerve is extremely small in size, being no more than two to three strands of cotton in thickness, and to find so small a nerve at a great depth following retraction of the carotid and jugular vessels and to identify it running down upon the posterior border of the stylopharyngeus is sometimes a matter of difficulty.

The only advantage that could be claimed for the high operation was that it was possible to avulse the ganglion on the nerve from the base of the skull, and that degenerative changes in this ganglion would sometimes be demonstrated at section.

Mr. Dickson Wright thought that Mr. Wilson's operation was very ingenious and simplified the approach to the nerve. If avulsion of the nerve was done in the neck operation and the two ganglia of the nerve were secured in this way a gush of cerebrospinal fluid usually followed. This avulsion prevented any possible recurrence of the malady and was worth doing and the leakage of cerebrospinal fluid caused no anxiety because the wound was tightly sutured.

Compression Neuritis of Both Median Nerves in the Carpal Tunnel: Surgical Decompression. Klippel-Feil Deformity of Neck. Sprengel Shoulder.—W. Russell Brain, D.M., and A. Dickson Wright, M.S.

E. W., married woman, aged 57. Two years' history of pain in front of right wrist spreading to thumb, index and middle fingers, like electricity, and associated with numbness in thumb, wasting of outer aspect of thenar eminence and weakness of thumb. Four weeks: Pain and paræsthesiæ in left thumb, index and middle fingers. Left shoulder always higher than right. Occasional pain in neck on extension.

Severe wasting and weakness of abductor brevis and opponens pollicis of right hand, and slight of left. Weakness of extension of right thumb at metacarpophalangeal and interphalangeal joints. Slight impairment of appreciation of light touch and pin-prick over distal half of palmar surfaces of thumb, index and middle fingers and radial half of ring finger of both hands and corresponding dorsal surfaces of terminal phalanges: no loss of tactile discrimination or postural sense. Sensory loss greater on right hand than left.

Electrical reactions.—Faradic response lost in right abductor brevis and opponens pollicis, and sluggish in abductor longus and the extensors of the thumb on both sides.

Neck very short; extension somewhat limited, some pain on lateral flexion. Prominence of lower cervical spinous processes. Left scapula higher than right.

X-rays (Dr. James Bull).—Fusion of cervical vertebræ except C3-C4 and C5-C6. Bilateral cervical ribs present. Left scapula is abnormally high and its vertebral border is angulated towards the spinal column in a "V" shape. At this point an

Comment.—The intracranial calcification is probably produced by calcareous degeneration in subependymal sclerotic nodules. The nature of the bony changes in tuberose sclerosis is obscure. Gottlieb and Lavine (1935) suggested that the lesions might be neurotrophic. Hall (1940) described bony lesions of two types, due to neurofibromatosis and rheostosis. Evidently tuberose sclerosis may occur in association with a generalized tissue dysplasia.

Glossopharyngeal Neuralgia treated by Trans-Tonsillar Section of the Nerve.—C. P. WILSON, C.V.O., F.R.C.S., and D. MCALPINE, M.D., F.R.C.P.

M. J., female aged 47. In June 1945 suddenly experienced a severe pain in the right ear when eating an apple. The pain lasted a few seconds. In August, during a meal, pain like "red hot needles" was felt at the back of the tongue on the right side. In subsequent attacks the pain shot up from the back of the tongue to the right ear. The pain was brought on by swallowing solids, liquids or even saliva. The frequency of the attacks gradually increased and by April 1946 they were recurring several times a day and even at night causing loss of weight and sleep.

14.5.46: Admitted Neurological Ward, Middlesex Hospital. Healthy woman with no abnormality in her nervous system apart from the right glossopharyngeal nerve. The attacks of pain during eating were confirmed. A trigger zone existed on the tonsil and adjacent surface of the tongue. The attacks of pain lasted about fifteen to thirty seconds. Cocainization of the trigger zone before meals almost completely abolished the pain.

5.6.46: Right tonsil removed by dissection and glossopharyngeal nerve exposed deep to tonsillar fossa. The nerve was divided and ⅜ in. was removed.

The patient has been completely free from pain since the operation and has gained over a stone in weight. There is loss of taste over the posterior third of the tongue on the right side and hypæsthesia over the distribution of the right ninth nerve.

Dr. D. McAlpine: This case shows characteristic features of glossopharyngeal neuralgia, the recognition of which we owe to Harris (1921), namely paroxysmal pain referred to the back of the tongue and the tonsil area, radiating to the ear, and in addition the existence of a trigger zone. The radiation of the pain is explained by the existence of the nerve of Jacobson which runs from the petrous ganglion to the tympanic plexus and thus to the tympanic membrane, middle ear and mastoid cells. The glossopharyngeal nerve does not supply the external auditory canal or the pinna, and in order to explain the occurrence of pain in these areas it is necessary to postulate an overflow along the auricular branch of the vagus which also takes origin from the petrous ganglion, or by the auriculotemporal branch of the trigeminal nerve which connects with the otic ganglion and thus indirectly with the glossopharyngeal nerve through the small superficial petrosal nerve.

The diagnosis of glossopharyngeal neuralgia is straightforward provided the situation and radiation of the pain and its relationship to swallowing is remembered. The diagnosis can be substantiated by cocainization of the tonsil area and back of the tongue, a procedure which relieves the pain.

Up to the present time operative treatment in severe cases has been limited to either (1) an intracranial resection of the ninth nerve using the suboccipital route, or (2) avulsion of the nerve high in the neck. Both of these operations are not devoid of risk. No previous report of a trans-tonsillar section of the nerve can be traced. The operation is a simple one in the hands of an experienced ear, nose and throat surgeon. In the present case the patient has been entirely free from pain for five months and there seems no reason why the result should not be permanent. In cases in which a trigger zone exists in the ear and not in the throat, it is probable that an intracranial operation may be necessary, but from our experience with the present case it would appear that if a trigger zone exists in the tonsil area then trans-tonsillar section of the nerve should be carried out. Only if such a measure fails to cure the pain should the intracranial approach be considered.

Mr. C. P. Wilson said that from the purely operative point of view the surgical procedure is quite simple. The tonsil is removed and the muscular layer in the tonsillar bed consisting of mixed fibres of the superior constrictor of the pharynx and palato-pharyngeus is divided. The nerve is found quite easily just outside the muscle layer in the lower part of the fossa as it passes forward to supply the posterior third of the tongue. It can quite easily be divided in this situation and as much of the nerve trunk can be removed as is felt necessary. There should be no very great difficulty in removing the nerve up as far as the base of the skull.

The type of case that I have previously dealt with is that in which the glossopharyngeal neuralgia is associated with an elongated styloid process pressing into the tonsillar bed and in these cases it deteriorate and the left eye to improve a little. Right vision disappeared completely by mid-June. At the same time the left leg became weak.

First seen in July 1946. She looked ill and had obviously lost weight. Temperature then running intermittently between 99°-101° F. There was extreme tenderness over the whole of the left scalp and also over the left temporo-mandibular joint so that she was unable to open her mouth properly. There was a superficial eruption over the left scalp. Both superficial temporal arteries were palpable but not pulsating.

V.A.—R. no P.L. L. J.6 corrected. Bilateral primary optic atrophy, the hazy margins of the discs being due to vitreous haze. Arteries markedly narrowed. Right pupil does not react directly to light. Left pupil does not react consensually. No gross field defect of left eye. Minor left spastic weakness with increased deep reflexes, ankle clonus, and an extensor-plantar response. No sensory defect.

Investigations.—Blood-count: R.B.C. 3,300,000; Hb. 60%: W.B.C. 5,000 with normal differential. E.S.R. (Wintrobe corrected) 22 mm. in one hour. W.R. negative in blood and C.S.F.

C.S.F.: Pressure 110 mm. Cells 3 lymphos. Protein 20 mg. Lange negative. X-ray of skull normal. Fractional test meal normal. Section of temporal artery shows recanalization of the previously thrombosed vessel lumen, with chronic inflammatory infiltration and occasional giant cells in the wall.

Progress.—There has been slow but steady improvement in the general condition with loss of tenderness of the scalp. There has, however, been no change in the physical signs. Temperature settled by the end of August, but the sedimentation rate was still 29 mm. at the beginning of September (*see* Cooke *et al.* 1946, Jennings 1938, Horton and Magath 1937).

Professor P. C. Cloake congratulated Dr. Kremer on his presentation of a case, which demonstrated most of the characteristic features of the disease. Many such cases must have gone unrecognized in the past.

He thought the pain in the back of the neck and left side of the head might have been due to involvement of the left occipital artery in the same process. Very frequently, as in this case, the ophthalmic arteries were affected, leading to optic atrophy and, in two of his own cases, definite signs of focal cerebral lesions were present, as well as mental changes, pointing to more diffuse disease.

He and his co-workers had drawn attention to the evidence of widespread affection of arteries in other parts of the body, giving rise to pain in muscles and joints and degeneration of peripheral nerves months or years before the appearance of temporal arteritis enabled the nature of the disease to be recognized.

The pathological change in the vessel wall was a focal necrosis of the media, with inflammatory reaction spreading from the adventitia to the media and tending to extend longitudinally. Giant-cell formation was present in foci of granulation tissue in the media, following upon the necrosis. Intimal thickening occurred and led on to thrombosis of smaller arteries. Veins were rarely affected.

The President stated that this was the first case of temporal arteritis that had been shown before this Section, but on account of its neurological interest it was probable that others would be shown in the future. As Professor Cloake had already pointed out, the process is more widespread than the name would suggest; in the case just shown the middle cerebral artery was involved. Published accounts of the disease had, on the whole, indicated a favourable prognosis, but in view of the nature of the arterial changes and their occurrence in elderly patients, it seemed that they would be subject to vascular accidents at a later date. In the cases reported by Cooke, Cloake and others, three of the patients died within two years of the onset of the disease, while only one patient made a good recovery.

Paget's Disease of the Skull with Platybasia.—JAMES BULL, M.B., M.R.C.P.

Housewife, aged 64, had noticed her head increasing in size for ten years. For seven or eight years she had become increasingly deaf, the right ear being more severely affected than the left. For one or two years she had had head noises and for over a year the right side of the face had been twitching. She complained of her head feeling heavy, and occasional unsteadiness in walking. The family history was not relevant.

On examination.—Head circumference 25¼ in. The frontal and temporal regions bulged particularly. Optic discs were normal, marked right-sided facial hemispasm abnormal bone articulates with the spinous process of C5 and with the vertebral border of the scapula.

Operation (October 14, 1946, by Mr. Dickson Wright).—The right median nerve was swollen for about half an inch above the carpal ligament and under the ligament. The carpal ligament was incised. The left median nerve was then exposed. This was also swollen but was pinker than the right. The left nerve divided into two parts about one inch above the upper end of the ligament both parts running together under the ligament. The ligament was incised and the wound sutured.

Dr. Russell Brain said that the syndrome of partial thenar atrophy was first described by Ramsay Hunt (1909, 1911, 1914) and subsequently by various observers, who had usually laid stress upon the absence of sensory disturbances. There was no evidence that it was due, as Hunt had suggested, to compression of the thenar branch of the median nerve where it turned back over the distal end of the transverse carpal ligament. Zachary (1945) had shown that a predominantly motor symptomatology could occur when the whole median nerve was compressed, as in these cases, in the carpal tunnel. The main diagnosis was from the costoclavicular syndrome, in which, though partial thenar atrophy might occur, sensory disturbances over the thumb and index finger were extremely rare.

Mr. A. Dickson Wright: The operation was done at the suggestion of Dr. Russell Brain who, in elucidating this syndrome, has clarified still one more form of "Neuritis". By discovering a mechanical cause for attrition of the median nerve he has made a most valuable contribution to neurology. The nerve was found to have responded to pressure and friction in the same useless way as elsewhere, viz. by swelling so that pressure and friction were increased and a vicious circle established which had to be broken by the operation of dividing the anterior carpal ligament from end to end so as to free the attrition. Similar situations were met with in disc lesions, cervical ribs and chafing of the ulnar nerve at the elbow. It was noticed at operation that the nerve was thickened for about two inches above the carpal ligament and there were characteristic pinkish and purplish colour changes in the nerve with marked increase in the fascicular markings. The extent of the swelling below the tunnel was not observed as it was not thought necessary to open up the palm but from experience it would be expected to find the swelling extending into the various branches of the nerve. Trouble in the form of prolapse of the flexor tendons seemed not to occur, presumably because the wrist is always in extension during gripping.

Dr. C. Worster-Drought said that he remembered rather an elaborate paper on the subject of "Partial Thenar Atrophy" by Wartenberg (1939) published shortly before the War. Wartenberg considered that the condition was more likely to occur when the branches of the median nerve supplying the outer part of the thenar eminence were abnormally situated. Wartenberg himself did not consider the condition due to a compression neuritis but apparently to general toxic factors acting on a group of muscles (opponens and abductor pollicis) that were phylogenetically of recent origin.

Most of the cases he (Dr. Worster-Drought) had seen did not show any sensory impairment over the area of median nerve supply but they might complain of localized paræsthesia. He considered that Dr. Russell Brain and Mr. Dickson Wright were to be congratulated on introducing a treatment for the condition. He assumed that the operative treatment they described would be more applicable to those cases showing definite sensory impairment or loss.

The President congratulated Dr. Brain on his presentation of this difficult case, and for bringing to their notice a new pathological explanation for certain cases of wasting of the thenar muscles. Dr. Brain had pointed out that the distribution of the wasting was similar to that found in certain types of cervical rib. The differential diagnosis would seem to lie in the distribution of the sensory loss and in the absence of vascular changes which were not unusual in cases of cervical rib.

Temporal Arteritis.—Michael Kremer, M.D., F.R.C.P.

Mrs. L. P., aged 75. In 1941 she developed malaise, night sweats, loss of weight, loss of appetite, and cough with some sputum. She was regarded as a tuberculosis suspect and kept under observation by the tuberculosis officer. X-ray of chest and sputum examination were negative, and she recovered completely in six months.

August 1945: Fell on the back of her head and since then has had tenderness of the occiput. No amnesia or other signs of intracranial damage. *March 1946:* Developed a severe pain spreading up the back of her neck and over the left side of the head. The scalp became extremely tender so that she was unable to sleep on the left side. Her general condition deteriorated and she began to run a temperature up to 101° F. June 1946: Vision deteriorated in the left eye, taking two to three days to diminish to light perception only. Ten days later the right vision began to such as that shown here, is quite obvious without resource to refined radiological methods of diagnosis. Platybasia in Paget's disease seldom causes symptoms of nerve or hind-brain pressure. This is true of the four cases observed by the author, and Moreton (1943) described six such cases in a series of 98 acquired platybasias. None of his six cases had signs of pressure from the basilar invagination. Ray (1942), on the other hand, described one case in a woman of 47 with an unsteady gait, a weak right arm and a dragging leg for a year. Suboccipital and upper cervical decompression improved her condition. Ray went so far as to say that it was likely that basilar deformity occurs in some degree in the majority of people with advanced Paget's disease.

The author demonstrated radiographs and diagrams illustrating the angle formed by the plane of the hard palate and that of the atlas. The difficulty of measuring the basilar angle of the skull was pointed out, in that the anterior end of the foramen magnum, an essential landmark in measuring the angle, is not visible in lateral radiographs owing to the superimposition of the mastoid processes. Furthermore (Lindgren, 1941) it is the occipital condyles, situated paramedially, and not the clivus, which first give way, and thus the basilar angle would not be altered in early basilar impression. Finally the empirical line drawn by Chamberlain (1939) from the back of the foramen magnum to the hard palate was stated by him to lie above the tip of the odontoid process of the axis. Saunders (1943), however, showed that 35 out of 100 normal cases which he examined had odontoid processes projecting above Chamberlain's line.

Professor P. C. Cloake said that he had not had an opportunity of testing Dr. Bull's method of diagnosing platybasia by measuring the angle referred to. He agreed that there was great difficulty in practice in measuring the so-called basal angle. He thought that in acquired cases the atlas did not always tilt forwards and upwards, as suggested by Dr. Bull, as the condylar processes of the occipital bone were pressed upwards into the cranial cavity and in congenital cases the arch of the atlas was sometimes fused with the occipital bone. These were purely theoretical objections to Dr. Bull's suggested method. They would have to be tested.

The criterion that the tip of the odontoid process of the axis was not cut by Chamberlain's line (the line joining the posterior end of the hard palate to superior posterior edge of the foramen magnum) in normal people also led to difficulty in diagnosing early cases of platybasia. The tip of the odontoid is difficult to identify with certainty in lateral films of the neck and it might appear to lie just below the line or just on it.

It was in the congenital cases of platybasia, often associated with congenital deformities of the cervical spine, that the diagnosis was of most value, because in those cases the deformity of the bones led to pressure upon the spinal cord or interference with its arterial circulation and also gross encroachment on the posterior fossa of the skull, leading to syndromes resembling cerebellar tumour, syringomyelia and amyotrophic lateral sclerosis, which might be relieved by decompression of the occipito-atlantal region.

Dr. Colin Edwards: It has been pointed out in America (Walsh *et al.*, 1941) that the term "platybasia" has been used by anthropologists to denote obtuseness of the sphenoidal angle beyond 150 degrees. This platybasia, however, causes no symptoms and is not necessarily associated with the invagination of the foramen magnum and its surrounding areas which does produce neurological symptoms. To this invagination the term "basilar impression" has been given and it is this basilar impression rather than platybasia which invites the attention of neurologists.

Dr. Redvers Ironside said that the transverse and antero-posterior diameters of the skull were much increased in the cases that he had seen. The vertical diameter measured from the margin of the foramen magnum to the vertex of the skull was diminished. This was caused by softening of the base of the occipital bone, which became pushed upwards by the vertebral column on which it rested. The cranial fossæ sagged, as it were, round the foramen magnum. Platybasia was therefore a usual finding in such cases.

Affection of the Trigeminal Nerve Nucleus and Central Grey Matter of the Spinal Cord following the Administration of Stilbamidine.—Major P. Collard, R.A.M.C., and Professor S. Nevin, M.D.

B., male, aged 23. Serving soldier. Complaint: Numbness of face.

History.—In April 1946 whilst he was serving in Salonika he fell ill and kala-azar was diagnosed. In July 1946 he was given a course of stilbamidine injections, total with involvement of the platysma. Right facial weakness. Spoken voice heard at 2 in. on right and 2 ft. on left; bone conduction better than air conduction. Forward bowing of left arm and some weakness of right arm. The trunk and lower limbs were normal, but the gait was rather unsteady.

Wassermann reaction negative. X-ray of skull: Bones of the vault were markedly thickened, about 2½ cm. The region of the foramen magnum was invaginated giving the skull a mushroom appearance. This change in shape was due to invagination of the occipital condyles, and as a result of this invagination the anterior portion of the atlas was pushed up. The plane of the atlas relative to that of the hard palate formed an angle of 42 degrees, the normal relationship being roughly parallel, the plane of the palate being slightly above that of the atlas. The angle is clearly seen in fig. 1.

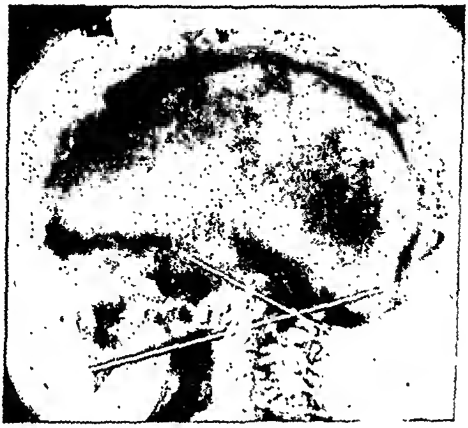


FIG. 1.

The appearances of the vault of the skull were characteristic of very advanced Paget's disease. All the bones surrounding the brain were involved, the disease process being most advanced in the frontal region where the new bone formation had a ray appearance suggesting the possibility of a sarcomatous degeneration. The bones of the face and both jaws were spared. The left humerus was the only other bone showing Paget's changes.

Mr. Wylie McKissock took a biopsy of the frontal bone.

Report (Dr. T. Crawford): The specimen shows bone trabeculæ with strands of cellular connective tissue infiltrating between them. There is active absorption of the trabeculæ going on and no laying down of new bone. The appearances are those of an osteitis deformans at an early stage. There is no evidence of sarcomatous change.

Observations.—The interest of the case was the complication of platybasia. Platybasia coming on in a previously normal-shaped skull—the acquired type—may be primary or secondary. The former group is the commoner, the cause is unknown and the texture of the bones of the skull is normal radiologically. Symptoms referable to the platybasia may or may not be present. The secondary platybasias, in which the cause is known, most commonly occur in Paget's skulls. (The author showed slides of three other cases which he had personally collected.) Theoretically any disease process involving softening of the occipital condyles might cause a secondary acquired platybasia, but apart from Paget's disease the author had only found a case of osteogenesis imperfecta in the literature. Platybasia may be commoner in Paget's disease than was formerly imagined and the early case may be more easily recognized by noting the plane of the hard palate relative to that of the atlas. The early case is not very easy to recognize, while the advanced case,

Section of Epidemiology and State Medicine

President—H. J. PARISH, M.D., F.R.C.P.E., D.P.H.

[*October* 25, 1946].

DISCUSSION ON HEALTH PROBLEMS IN GERMANY.

Colonel T. F. Kennedy: As Deputy Chief of the Public Health Branch of Supreme Headquarters, Allied Expeditionary Force, later as Director of Public Health (Civil Affairs) 21st Army Group and finally as Principal Medical Officer of the I., A. and C. Division of the Control Commission for Germany (British Element) I had the privilege of being able to follow the trend of events from the planning stage for civil health problems in the North-West European campaign to the completion of one year's occupation of our Zone in Germany.

I will start with the crossing of the Rhine and try to map out briefly the main measures which were taken to safeguard the health of the civil population and to prevent the spread of infectious disease.

Information had been received that typhus fever was more or less widely seeded throughout Germany. It was therefore necessary that we should have a plan to control the movement westward to their home countries of the vast numbers of displaced persons likely to be uncovered by the advancing armies.

It was decided that the main waterways traversing the country from north to south, in which the majority of the bridges would undoubtedly be destroyed, would form the best barriers. Control disinfestation centres were therefore set up at the following lines in succession: Rhine-Ijssel, Dortmund-Ems Canal, River Weser and River Elbe. The disinfestation centres were supplied with hand and power powder dusters and 10% D.D.T. powder was liberally dusted on all civilians presenting themselves at the crossings of these waterways.

The results obtained were amazingly good. A certain number of typhus-infected persons filtered through these barriers in the incubation period and developed the disease either *en route* or at their destinations. The passage of these cases was unavoidable short of instituting quarantine stations which was quite impracticable. Of about 1½ million displaced persons who were evacuated westward in the first few months the number of secondary infections, arising as a result in the liberated countries of Western Europe which received them, was surprisingly small.

We had put our faith in D.D.T. and it certainly proved to be a most effective weapon in the control of typhus. One recalls the devastating epidemics of typhus fever during, and after, the 1914-1918 war and one shudders to think what might have happened in Western Europe had we not had D.D.T. at our disposal.

A small public health staff was operating under 21st Army Group (Civil Affairs) whose duty it was to rehabilitate the Civil Health Administrations, and to give such help as was practicable to them, as soon as possible after territories were uncovered by the advance. These Public Health Officers were earmarked for their particular role in the Military Government of Germany, and were deployed to their respective stations as soon as possible so that when the fighting ceased the majority of them were already at their posts and had started work on the rehabilitation of the German Health Services.

The British Zone of Germany consists of the provinces of Schleswig-Holstein, Hanover, Westphalia and North Rhine provinces.

These provinces are divided into varying numbers of Regierungsbezirke which in turn are further subdivided into Stadt and Land Kreise.

We had British Public Health Staffs at Provincial and at Regierungsbezirk levels dosage 0·6 gramme. His kala-azar cleared up and he was quite well until the beginning of October 1946 when one morning he noticed numbness over the tip of his nose and upper lip. One day later the numbness had spread up to around the eyes, and three days later the whole face and forehead were numb.

When first seen on October 10, 1946, his general condition was good, and the only abnormal signs in the C.N.S. were found in the trigeminal nerve, as follows: Sensation: Dulling to pin-prick and impaired perception of light touch and heat and cold, in all three divisions of the fifth nerve on both sides: 2 point discrimination, deep pain, and vibration sense were intact. Motor n.a.d. Corneal reflexes present and equal. Jaw-jerk present.

Ten days later the sense of numbness spread down into the neck and over the back of the scalp the lowest dermatome affected being C3. Since then there has been a gradual improvement in that the sensory loss has become both less extreme and less severe.

Present condition.—Neurological signs are limited to the fifth nerve. Motor and reflex functions of this nerve are normal. The sensory disturbance is as follows: There is dulling to pin-prick and impaired perception of light touch in all three divisions on both sides, otherwise there is no abnormality.

Professor S. Nevin: There can be little doubt that the lesion in these cases is in the fifth nerve nucleus and in the central grey matter of the cervical spinal cord. We have here, then, another of these examples of selective action on the nervous system which are always very interesting, but very difficult to explain. The nuclei affected are the chief pontine nucleus and the descending nucleus, and the cells in these nuclei are different structurally from the mesencephalic root of the fifth nerve which appears to be intact, as is shown by the preservation of the jaw-jerk. The other interesting point is that the symptoms set in three months after the injections. How can this long latent period be explained? It is possible that the drug is fixed by the cells and that a toxic substance is liberated later by metabolic changes. It is perhaps possible that it is absorbed at the sensory nerve-endings and produces the lesion when it reaches the cell bodies.

Dr. J. W. Aldren Turner: This trigeminal neuropathy following the use of stilbamidine is common, so common that the use of the drug in the treatment of kala-azar has been prohibited in India Command. Stilbamidine is diamidino-diphenyl-ethylene, and it is probably the ethylene linkage which is important in the production of the trigeminal affection, as this radical is also present in trilene, which causes cranial nerve palsies at times, when it is used as an anæsthetic in a closed circuit. The other diamidine used in tropical medicine, propamidine, is also toxic to the nervous system and causes a peripheral neuritis but apparently does not affect the trigeminal nerve and there is no ethylene linkage in this compound.

In two personally studied cases of stilbamidine neuropathy there has been dissociated sensory loss in the trigeminal distribution, appreciation of pain and temperature being normal but light touch being impaired, which suggests that the lesion is in the principal sensory nucleus of the trigeminal nerve. In addition the patients had coarse involuntary twitching movements of the upper lip.

The President agreed with Dr. Aldren Turner that in India the condition was not uncommon. Napier and Sen Gupta (1942); Sen Gupta (1943) had met with it in 18 out of a total of 108 cases of kala-azar treated with this drug.

REFERENCES

CHAMBERLAIN (1939) *Yale J. Biol. Med.*, **11**, 487.
COOKE, W. T., CLOAKE, P. C., GOVAN, A. D. T., and COLBECK, J. C. (1946) *Quart. J. Med.*, **15**, 47.
GOTTLIEB, J. S., and LAVINE, G. R. (1935) *Arch. Neurol. Psych., Chicago*, **33**, 379.
HALL, G. S. (1940) *Quart. J. Med.*, **33**, 1.
HARRIS, W. (1921) *Brit. med. J.* (ii), 896.
HORTON, B.T., and MAGATH, T. B. (1937) *Proc. Mayo Clin.*, **12**, 43.
HUNT, J. R. (1909) *Trans. Amer. neurol. Ass.*, **35**, 184.
—— (1911) *Amer. J. med. Sci.*, **141**, 224.
—— (1914) *Rev. Neur. Psychiat.*, **12**, 137.
JENNINGS, G. H. (1938) *Lancet* (i), 424.
LINDGREN, E. (1941) *Acta Radiol.*, **22**, 297.
MORETON (1943) *Proc. Mayo Clin.*, **18**, 353.
NAPIER, L. E., and SEN GUPTA, P. C. (1942) *Ind. med. Gaz.*, **77**, 71.
RAY, B. S. (1942) *Ann. Surg.*, **116**, 231.
SAUNDERS, W. W. (1943) *Radiology*, **41**, 589.
SEN GUPTA, P. C. (1943) *Ind. med. Gaz.*, **78**, 537.
WALSH, M. N., CAMP, J. D., and CRAIG, W. M. (1941) *Proc. Mayo Clin.*, **16**, 449.
WARTENBERG, R. (1939) Partial Thenar Atrophy, *Arch. Neurol. Psych.*, **42**, 373.
ZACHARY, R. B. (1945) *Surg. Gynec. Obstet.*, **81**, 213.

Section of Epidemiology and State Medicine

President—H. J. PARISH, M.D., F.R.C.P.E., D.P.H.

[*October* 25, 1946].

DISCUSSION ON HEALTH PROBLEMS IN GERMANY.

Colonel T. F. Kennedy: As Deputy Chief of the Public Health Branch of Supreme Headquarters, Allied Expeditionary Force, later as Director of Public Health (Civil Affairs) 21st Army Group and finally as Principal Medical Officer of the I., A. and C. Division of the Control Commission for Germany (British Element) I had the privilege of being able to follow the trend of events from the planning stage for civil health problems in the North-West European campaign to the completion of one year's occupation of our Zone in Germany.

I will start with the crossing of the Rhine and try to map out briefly the main measures which were taken to safeguard the health of the civil population and to prevent the spread of infectious disease.

Information had been received that typhus fever was more or less widely seeded throughout Germany. It was therefore necessary that we should have a plan to control the movement westward to their home countries of the vast numbers of displaced persons likely to be uncovered by the advancing armies.

It was decided that the main waterways traversing the country from north to south, in which the majority of the bridges would undoubtedly be destroyed, would form the best barriers. Control disinfestation centres were therefore set up at the following lines in succession: Rhine-Ijssel, Dortmund-Ems Canal, River Weser and River Elbe. The disinfestation centres were supplied with hand and power powder dusters and 10% D.D.T. powder was liberally dusted on all civilians presenting themselves at the crossings of these waterways.

The results obtained were amazingly good. A certain number of typhus-infected persons filtered through these barriers in the incubation period and developed the disease either *en route* or at their destinations. The passage of these cases was unavoidable short of instituting quarantine stations which was quite impracticable. Of about 1½ million displaced persons who were evacuated westward in the first few months the number of secondary infections, arising as a result in the liberated countries of Western Europe which received them, was surprisingly small.

We had put our faith in D.D.T. and it certainly proved to be a most effective weapon in the control of typhus. One recalls the devastating epidemics of typhus fever during, and after, the 1914-1918 war and one shudders to think what might have happened in Western Europe had we not had D.D.T. at our disposal.

A small public health staff was operating under 21st Army Group (Civil Affairs) whose duty it was to rehabilitate the Civil Health Administrations, and to give such help as was practicable to them, as soon as possible after territories were uncovered by the advance. These Public Health Officers were earmarked for their particular role in the Military Government of Germany, and were deployed to their respective stations as soon as possible so that when the fighting ceased the majority of them were already at their posts and had started work on the rehabilitation of the German Health Services.

The British Zone of Germany consists of the provinces of Schleswig-Holstein, Hanover, Westphalia and North Rhine provinces.

These provinces are divided into varying numbers of Regierungsbezirke which in turn are further subdivided into Stadt and Land Kreise.

We had British Public Health Staffs at Provincial and at Regierungsbezirk levels but not at Kreis levels. A Regierungsbezirk is roughly comparable to a County in England.

The work of these Officers in getting the German Health Services on their feet again was rendered very difficult by massive destruction of hospitals and public services which had been caused by the bombing and fighting, by the chaos which prevailed after defeat and capitulation, by the almost complete lack of communications and by the fact that the majority of the senior Public Health officials and other senior professional medical men had to be relieved of their duties on account of their Nazi associations. The result was that the inexperienced man of inferior professional capacity had to be relied on in the building up of the health services. There was, however, no shortage in numbers of doctors, and releases from the Wehrmacht of medical men often produced an embarrassing situation in which, in certain localities, there were more doctors than were required.

In spite of these difficulties slow but steady progress was made. There was a shortage of medical supplies and immediate steps were taken for priority to be given to the starting up of factories producing them.

Hospital accommodation was very inadequate. Many hospitals had been destroyed—many others seriously damaged. A comprehensive plan was drawn up to increase the number of hospital beds and, as a result, the number was raised from 0·8% of population to well over 1%, with provision for expansion by another 0·3% by the winter of 1945. This meant an increase of approximately 100,000 beds.

In the cities and larger towns serious disruption of the water and sewage installations was almost universally present. This required strenuous measures to prevent the occurrence and spread of water-borne diseases.

Reliable statistical data on the state of the health of the population were not available for some time after the occupation of Germany, due to the causes already mentioned, such as disorganization of the health services, loss of records and almost complete disruption of communications. It was evident, however, that tuberculosis had increased considerably during the war years, though its extent has not been definitely ascertained and, short of mass radiography, it is doubtful if it will be. Diphtheria was prevalent. The incidence in the British Zone for the last quarter of 1945 was from 80/100 per 10,000 per annum in the North Sea and West Baltic areas which include Berlin, Schleswig-Holstein, Hamburg, Bremen and Hanover. The rest of the British Zone was about half this rate. The average case mortality was 5·7%. Typhoid was also fairly widespread but the number and extent of epidemics were far less under the conditions prevailing than one had anticipated. A few sporadic cases of poliomyelitis occurred.

The main hazards of health might be summarized under the following headings: (1) Inadequate nutrition. (2) Lack of adequate accommodation owing to the enormous destruction of houses and to increase of population caused by migration from the East. (3) Massive destruction and damage to water and sewage undertakings.

The state of nutrition of the civil population was kept constantly under review and was the subject of repeated nutritional surveys. Practically all food was rationed and our aim was that the ration scale should at least provide the minimum food necessary for the bare maintenance requirements of health. This was laid down at 1,550 Cals. for the normal adult consumer. This scale was not reached during the first year of occupation of the British Zone. 1,250 Cals. was attained but this had to be reduced early this year to 1,050 at which scale it was when I left Germany in May 1946. I understand that it has since been increased to 1,250 Cals. and that it is hoped to reach a 1,550 Cal. scale before long.

In spite of this extremely low and inadequate ration scale there were few indications of serious deterioration in the nutritional health of the normal consumer. The only explanation I can offer for this is that the ration scale must have been considerably supplemented from one source or another.

There was, however, evidence of nutritional deficiency in institutions, where supplementation of the ration scale was difficult; in aged people and others who were unable to forage for extra food; and in children. There was also a considerable loss of weight in adults compared with twelve months previously. It was common to find men and women who had lost as much as 30 to 40 lbs. This is not surprising for the Germans were habitually overweight in pre-war days. Special ration scales were issued to children, adolescents, pregnant women, moderately heavy workers, heavy workers and very heavy workers.

It was always felt and constantly stressed that a diet sufficient for the normal requirements of the body must necessarily form the basis on which the general health of the population is founded.

The accommodation problem was governed by two main factors: (1) Increase in population. (2) Destruction of houses.

The total population of the British Zone in 1939 was approximately 20 millions. In September 1945 it was slightly more but the numbers of displaced persons to be repatriated would bring it down to about 20 millions again. In addition, plans had to be made for the reception of a possible 3¾ million refugees from the East.

In 1939 there were 5,459,000 dwelling houses in that part of Germany which is now the British Zone. Of these, approximately 2,000,000 were destroyed and 1,000,000 were damaged, leaving approximately 2,500,000 undamaged. Of the damaged houses about 600,000 were capable of being made habitable for the winter. The number of dwellings, therefore, capable of habitation during the winter of 1945-1946, was in the region of 3,000,000. If one allows 420 sq. ft. of living space per dwelling, the habitable houses in the Zone would permit of 53 sq. ft. of floor area per person for the projected population of 23,750,000.

Certain areas were tentatively earmarked as "Black Areas" in relation to the plan for the reception of refugees from the East. The earmarked areas were: (1) The whole area of the British Zone west of the Rhine. (2) The area of the Ruhr Regional Planning Authority. (3) The towns of Münster, Paderborn, Hanover, Wilhelmshaven, Emden, Hamburg, Lübeck, Neumünster, Kiel, Flensburg, Schleswig, Lütjenburg, Eutin, Lüneburg and Braunschweig.

The distribution of refugees from the East was thus based on a survey of the accommodation available and they were distributed on that basis.

One cannot leave the subject of accommodation without referring to the shortage of fuel for cooking and ordinary domestic heating. Owing to the diminished output of the coalmines of the Ruhr and elsewhere and the increased demands for reparation on such as was produced, no coal was allowed for domestic consumption to the civil population. The civil population had to make such arrangements as they could for the felling of timber and the collecting of wood fuel from the countryside. The result was that in the majority of cases it was difficult to obtain sufficient fuel for cooking and little was available for domestic heating.

With such a bleak prospect in regard to accommodation it was doubly necessary to increase hospital beds throughout the Zone to a figure which might be capable of dealing with the number of patients which might reasonably be expected from a population badly housed and insufficiently fed. The increase of hospital beds, previously mentioned, of 100,000 was consequently effected. The manufacture and distribution of essential medical supplies were speeded up and stocks of one month's requirement of these were accumulated at selected centres so that they might be readily available in an emergency. Medical, nursing and auxiliary personnel were earmarked for their respective duties and in each Regierungsbezirk 5% of doctors and trained nurses were specially earmarked to be formed into mobile teams of 1 doctor and 3 trained nurses for emergency service in any part of the Zone. These teams were to be provided from local resources, with a scale of medical equipment but not at Kreis levels. A Regierungsbezirk is roughly comparable to a County in England.

The work of these Officers in getting the German Health Services on their feet again was rendered very difficult by massive destruction of hospitals and public services which had been caused by the bombing and fighting, by the chaos which prevailed after defeat and capitulation, by the almost complete lack of communications and by the fact that the majority of the senior Public Health officials and other senior professional medical men had to be relieved of their duties on account of their Nazi associations. The result was that the inexperienced man of inferior professional capacity had to be relied on in the building up of the health services. There was, however, no shortage in numbers of doctors, and releases from the Wehrmacht of medical men often produced an embarrassing situation in which, in certain localities, there were more doctors than were required.

In spite of these difficulties slow but steady progress was made. There was a shortage of medical supplies and immediate steps were taken for priority to be given to the starting up of factories producing them.

Hospital accommodation was very inadequate. Many hospitals had been destroyed—many others seriously damaged. A comprehensive plan was drawn up to increase the number of hospital beds and, as a result, the number was raised from 0·8% of population to well over 1%, with provision for expansion by another 0·3% by the winter of 1945. This meant an increase of approximately 100,000 beds.

In the cities and larger towns serious disruption of the water and sewage installations was almost universally present. This required strenuous measures to prevent the occurrence and spread of water-borne diseases.

Reliable statistical data on the state of the health of the population were not available for some time after the occupation of Germany, due to the causes already mentioned, such as disorganization of the health services, loss of records and almost complete disruption of communications. It was evident, however, that tuberculosis had increased considerably during the war years, though its extent has not been definitely ascertained and, short of mass radiography, it is doubtful if it will be. Diphtheria was prevalent. The incidence in the British Zone for the last quarter of 1945 was from 80/100 per 10,000 per annum in the North Sea and West Baltic areas which include Berlin, Schleswig-Holstein, Hamburg, Bremen and Hanover. The rest of the British Zone was about half this rate. The average case mortality was 5·7%. Typhoid was also fairly widespread but the number and extent of epidemics were far less under the conditions prevailing than one had anticipated. A few sporadic cases of poliomyelitis occurred.

The main hazards of health might be summarized under the following headings: (1) Inadequate nutrition. (2) Lack of adequate accommodation owing to the enormous destruction of houses and to increase of population caused by migration from the East. (3) Massive destruction and damage to water and sewage undertakings.

The state of nutrition of the civil population was kept constantly under review and was the subject of repeated nutritional surveys. Practically all food was rationed and our aim was that the ration scale should at least provide the minimum food necessary for the bare maintenance requirements of health. This was laid down at 1,550 Cals. for the normal adult consumer. This scale was not reached during the first year of occupation of the British Zone. 1,250 Cals. was attained but this had to be reduced early this year to 1,050 at which scale it was when I left Germany in May 1946. I understand that it has since been increased to 1,250 Cals. and that it is hoped to reach a 1,550 Cal. scale before long.

In spite of this extremely low and inadequate ration scale there were few indications of serious deterioration in the nutritional health of the normal consumer. The only explanation I can offer for this is that the ration scale must have been considerably supplemented from one source or another.

nucleus of representation of the health services in the British Zone in a central Health Administration for the whole of Germany if and when such an administration eventualizes.

In Berlin a quadripartite Health Committee was set up which dealt with such health problems as were common to all the four Zones, British, American, Russian and French. Information on health matters was also exchanged at this level.

Any reference to the work which has been carried out on health in Germany would be incomplete without a warm tribute to the sound planning carried out by the Health Branch of S.H.A.E.F. under Major-General Warren F. Draper, C.B.E., of the United States Army, to the whole-hearted, self-sacrificing and most efficient service rendered by the personnel of the Health Branch of the Control Commission, and to the invaluable assistance which was given to us by the Army Medical Services under Major-General Sir Edward Phillips, K.B.E., without whose help in the early days we could not have succeeded in our task.

Dr. P. G. Horsburgh (*late Lieut.-Colonel, R.A.M.C.*): *Berlin at the time of occupation.*—Before entering Berlin we had information as to the portion we were to control. Berlin would be divided into three roughly equal parts, to be occupied by the U.S.A., U.S.S.R. and ourselves: the population of each was approximately 1 million.

It should be appreciated that Berlin was over 100 miles from the British Zone of Germany. It was completely isolated in the Russian Zone except for the autobahn for military traffic and a single line railway which was under Russian control—the second track having been pulled up by the Russians for some unknown reason. The lack of communication with our Zone made for difficulties of supply, such as food, drugs, &c.: German civilian transport required Russian permits which were nearly impossible to obtain for the first three months of our occupation.

We are here only concerned with the medical section of the Military Government. This was, on entry, the smallest section in number of any section of Military Government, consisting of myself and one gunner (a clerk). This was, fortunately, rectified in a few weeks time after the appalling conditions and problems were realized by the powers that be.

One did not require to be a medical man to appreciate the very bad state of health of the Berlin people, even allowing for the bombing and fighting that had gone on in the city. In no area I had been in, such as the hard-hit Ruhr, had people shown such malnutrition. These conditions were obvious on entering the city.

Our first job was to contact our allies. The U.S.A. Health Section was well known as we had been working together in other areas. The Red Army were unknown. It took some time to make contact with our Soviet opposite numbers. The first attempt is too long a story to relate here, suffice to say we learnt the Russian word "no"—with a sub-machine gun pointing at us in a most disconcerting manner.

After some days we did create a joint meeting of the Allied Public Health Officers. These meetings were long and difficult owing to the distrust shown at first by the Red Army. Our first difficulty, for example, was that the water supply, being greatly contaminated, had to be made safe. The water supply to Berlin is from shallow wells fed from the lakes round the city. The water is filtered by sand filters, but not as a whole chlorinated. There were some three to four thousand major breaks in the water system and two to three thousand in the sewage system. The electricity supply was very intermittent, causing failure in the pumps with a loss of water pressure and in fact causing negative pressure. It was suggested that all water should be heavily chlorinated in the whole of the city. U.S.A. agreed, but to our astonishment the Russians refused point blank to agree to a general order. They maintained that an order to the Germans should be made to obtain a pure which was based on the minimum requirement for the treatment (either hospital or domiciliary) of 100 patients for one week.

The winter of 1945-1946 passed, fortunately, without any serious epidemic but the hospital situation throughout the Zone had been placed on a sound footing, capable of meeting any ordinary demands, and the handing over by the British Military Authorities to the German Civil Authorities of all the Wehrmacht patients and hospitals provided still more hospital accommodation.

The immigration of refugees from the Russian Zone and from that part of Germany taken over by Poland presented serious problems in controlling the introduction of infectious disease. Certain refugee reception centres were set up at selected points on the frontier between the British and Russian Zones. At these centres refugees were fed, given ration cards, medically inspected and dusted with D.D.T. powder.

It was quite impracticable to install an effective barrier all along the frontier so reliance had to be placed on making it to the advantage of the refugees to come through the selected centres. The provision of shelter, food, ration cards and onward transport to their destinations provided the necessary attraction and very few refugees crossed the "green" frontier between the centres.

The responsibility for medical examination of the refugees, hospitalization, segregation and dusting with D.D.T. was put on the German Health Services under the general supervision of the British Public Health Staffs.

Courses of instruction in D.D.T. dusting had been set up in each Province for German personnel and eventually every Stadt and Land Kreis had persons trained in the technique and had the equipment necessary for carrying out the dusting.

By this means all refugees arriving at the frontier were dusted and they were dusted again on arrival at their final destination within the Zone. Any cases of typhus imported during the incubation period were promptly and adequately dealt with wherever they occurred, contacts were dusted, and secondary infections were kept at negligible proportions.

The extensive damage to water and sewage installations in the cities and larger towns was such a potential hazard to health that early priority was given to their repair and every effort was made to provide the raw material necessary. Immediate steps were taken for super-chlorination of water supplies to be carried out so as to ensure that available chlorine was always present in the water delivered at all distribution points on the supply system. These measures were effective and I am aware of only two instances in which outbreaks of disease—both enteric—were considered to be due to water-borne infection.

During the first few months after occupation the responsibility for rehabilitation and direction of the German Health Services necessarily devolved on the British Public Health Staff of the Control Commission but the policy was that this responsibility should gradually be handed over to the Germans themselves as soon as they were in a position to assume it. Our officers at Provincial and Regierungsbezirk Headquarters dealt with the German Health Administrative Officers at these levels and the administrative channels for instruction and information passed through them. In this way control and intimate contact with German Health Administration in the field were effected but the executive work was the responsibility of the Germans themselves. In order to promote the handing over of responsibility to the Germans a German Zonal Advisory Committee on Public Health was formed of representatives of each of the Provinces within the Zone and it gave valuable assistance to the Public Health Staff of the Control Commission on the many problems put before it, including the control of the medical and nursing services, medical and nursing education, medical supplies and distribution, venereal disease, &c.

This Committee remained advisory up to the time I left Germany but it was hoped that it would eventually be given executive powers and that it would form the nucleus of representation of the health services in the British Zone in a central Health Administration for the whole of Germany if and when such an administration eventualizes.

In Berlin a quadripartite Health Committee was set up which dealt with such health problems as were common to all the four Zones, British, American, Russian and French. Information on health matters was also exchanged at this level.

Any reference to the work which has been carried out on health in Germany would be incomplete without a warm tribute to the sound planning carried out by the Health Branch of S.H.A.E.F. under Major-General Warren F. Draper, C.B.E., of the United States Army, to the whole-hearted, self-sacrificing and most efficient service rendered by the personnel of the Health Branch of the Control Commission, and to the invaluable assistance which was given to us by the Army Medical Services under Major-General Sir Edward Phillips, K.B.E., without whose help in the early days we could not have succeeded in our task.

Dr. P. G. Horsburgh (*late Lieut.-Colonel, R.A.M.C.*): *Berlin at the time of occupation.*—Before entering Berlin we had information as to the portion we were to control. Berlin would be divided into three roughly equal parts, to be occupied by the U.S.A., U.S.S.R. and ourselves: the population of each was approximately 1 million.

It should be appreciated that Berlin was over 100 miles from the British Zone of Germany. It was completely isolated in the Russian Zone except for the autobahn for military traffic and a single line railway which was under Russian control—the second track having been pulled up by the Russians for some unknown reason. The lack of communication with our Zone made for difficulties of supply, such as food, drugs, &c.: German civilian transport required Russian permits which were nearly impossible to obtain for the first three months of our occupation.

We are here only concerned with the medical section of the Military Government. This was, on entry, the smallest section in number of any section of Military Government, consisting of myself and one gunner (a clerk). This was, fortunately, rectified in a few weeks time after the appalling conditions and problems were realized by the powers that be.

One did not require to be a medical man to appreciate the very bad state of health of the Berlin people, even allowing for the bombing and fighting that had gone on in the city. In no area I had been in, such as the hard-hit Ruhr, had people shown such malnutrition. These conditions were obvious on entering the city.

Our first job was to contact our allies. The U.S.A. Health Section was well known as we had been working together in other areas. The Red Army were unknown. It took some time to make contact with our Soviet opposite numbers. The first attempt is too long a story to relate here, suffice to say we learnt the Russian word "no"—with a sub-machine gun pointing at us in a most disconcerting manner.

After some days we did create a joint meeting of the Allied Public Health Officers. These meetings were long and difficult owing to the distrust shown at first by the Red Army. Our first difficulty, for example, was that the water supply, being greatly contaminated, had to be made safe. The water supply to Berlin is from shallow wells fed from the lakes round the city. The water is filtered by sand filters, but not as a whole chlorinated. There were some three to four thousand major breaks in the water system and two to three thousand in the sewage system. The electricity supply was very intermittent, causing failure in the pumps with a loss of water pressure and in fact causing negative pressure. It was suggested that all water should be heavily chlorinated in the whole of the city. U.S.A. agreed, but to our astonishment the Russians refused point blank to agree to a general order. They maintained that an order to the Germans should be made to obtain a pure water supply. This was not done from lack of knowledge, but because it involved the U.S.S.R. getting from either U.S. or ourselves chlorine of which they had none. The difficulty was got over and the water was chlorinated. This small argument lasted three weeks.

The Military Government became greatly improved on the formation of a body, known as the Kommandatura, consisting of Commandants of each Allied power and the necessary Committee of each function working under them. This Committee (in our case the Public Health Committee) passed recommendations to the Commandants and they passed orders to the German Magistrat.

The German administration was left unchanged by the Allied powers. The Magistrat of the City includes a Public Health Department headed by a Medical Officer of Health.

The City is divided into 20 districts or Bezirke each with a Burgomaster and its Health Department. These have not the power of a London Borough, as they come under the general control of the Magistrat and do not raise a separate rate.

I would remind you that the City had capitulated to the Red Army on May 2, consequently the German Officers at the Magistrat and the districts on our entry were holding posts with Russian consent.

Of the six districts we took over, all Medical Officers of Health, except one, had been appointed, not for their ability but for their political views: suffice it to say that one was not even a medical man and another had "done time" for illegal operations. Drastic action was immediately taken and one month after British Military Government was established efficient medical officers were in each district of the British Sector.

Although British troops moved in on July 4 British Military Government did not take over its sector till July 12, 1945. During this time one found certain conditions, namely: (1) Polluted water supply. (2) Sewage system—20% going into sewage works only. 80% flowing into rivers and canals in the centre of the city. (3) Major epidemics of dysentery. (4) Shortage of medical supplies, some large hospitals having as little as one pint of ether and no sulphonamide. (5) Inadequate food supplies, no salt, and ration cards not being honoured. (6) High V.D. rate. (7) Major fly nuisance. (8) Shortage of hospital beds, 5,000 for the area, 50% of which were unfit for use in rain or cold.

These conditions applied to the city as a whole and should obviously be treated by uniform measures. These uniform measures should have been taken by agreement of the Allied Public Health Committee. (At the end of August the French took over a portion of the British Sector, and the committee then became quadruplicate.)

The hospital problem gave us great concern. As already mentioned, we had some 5,000 beds in our area, all the hospitals being damaged to a major degree. To increase the number of beds, repairs had to be pushed forward and other new buildings utilized by repairs and conversions. With the great help of the R.E.s attached to Military Government a special German Labour Force was brought in from the Zone and hospitals were put on No. 1 repair priority. The difficulties were many but were overcome; for example, glass was just not available. We found, however, that the Central Store of X-ray Films of the Insurance Organization of Germany was housed in Berlin in the British Sector and practically undamaged. Although these were valuable records I considered it more important to have them cleaned and use them instead of glass. These were used, but before we could utilize them we had to fly in nails as there were no nails in the city. It is interesting to record that every hospital of any size had a deep operating theatre block and beds for 6 or 7 patients, and in no instance did we find one of these deep units damaged by bombs. The Germans had in Berlin large surface air-raid shelters (bunkers). These could house some thousands of people, they were 4- to 5-storey structures with 7 feet reinforced walls, air conditioned and lifts to all floors. These had withstood the bombing and we converted one into a very good 3 to 4 hundred-bedded hospital. By the time Colonel Raeburn and I left Berlin in April we had over 9,000 weatherproof beds in operation, and emergency accommodation for 2,000 beds which could have been equipped and staffed in ten days if required. The staffing of the hospitals was not a difficult problem. We had in the British Sector a higher proportion of medical men than the other sectors.

On the de-nazification of the medical profession we are open to criticism. We did not pursue this problem with that energy that occurred in the other sectors. It was feared that Berlin might become more of the plague spot than it already was. We had orders to be ready for the "battle of the winter". No definite de-nazification law had been agreed till this year. I thought it best to get rid of the real red-hot Nazi, but not the nominal members. The U.S. were quite ruthless in getting rid of the nominal members, with the result they had great difficulty in staffing hospitals, domiciliary treatments, &c. When the de-nazification law was agreed they had to reinstate medical personnel that they had previously debarred from practice. We were, I think, justified in our more moderate action.

The question of domiciliary treatment of the German civilian caused difficulties, not from the point of view of numbers of doctors, but from the point of transport. The number of cars available for doctors in the British Sector was in the region of 10. It was obvious that doctors could not visit their normal districts. We, therefore, divided the British Sector into small districts by which it was possible for the doctor to walk to the patients.

Transport, or lack of it, caused difficulties in admitting patients to hospital. We had 7 ambulances of ancient vintage and 4 in the Russian Sector, i.e. 11 ambulances for 3 million population. Patients had to be taken to hospital in hand carts, horse vehicles, and the like, many dying before their arrival.

This difficulty was overcome by bringing into Berlin 20 ambulances from the Zone, 16 of which were ex-German army ambulances and 4 new British vehicles. These ambulances could not be used in the Russian Sector as permits could not be obtained from the Red Army. The treatment of patients, both surgical and medical, was a major difficulty on account of shortage of drugs, dressings, &c. The medical supplies in all hospitals and for general practitioners were such that much unnecessary suffering and loss of life were taking place. The death-rate was estimated to be in the region of 60 per thousand of the population and the infant mortality rate about 300 per 1,000 live births. These estimated figures may possibly be on the low side.

Sulphonamides were practically non-existent, even in the hospitals. Anæsthetics also were so short that surgeons had in many cases to stop, or drastically curtail their work. We endeavoured to get an agreement with our Allies as regards getting medicaments into the city. The Russians would not agree to work this on a city-wide level. The position was so acute it was decided by U.S. and ourselves that we would each bring in medicaments for our own sectors—an unsatisfactory arrangement but the only one which could be carried out quickly. It was decided in British and U.S. Sectors to set up medical stores and such a store was forthwith set up in the British Sector with a German Staff.

Owing to the extensive black market in drugs (U.S. penicillin one ampoule would fetch £75) it was decided to issue only to the hospitals in the British Sector. The amount of drugs brought in by December was something over 500 tons. The hospitals by November were well supplied with drugs and it was thought advisable to allow dispensing of private practitioners' prescriptions at the hospitals, when the drugs could not be obtained through chemists. A certain intermittent supply of drugs was coming into the city, through normal trade channels, by November 1945.

water supply. This was not done from lack of knowledge, but because it involved the U.S.S.R. getting from either U.S. or ourselves chlorine of which they had none. The difficulty was got over and the water was chlorinated. This small argument lasted three weeks.

The Military Government became greatly improved on the formation of a body, known as the Kommandatura, consisting of Commandants of each Allied power and the necessary Committee of each function working under them. This Committee (in our case the Public Health Committee) passed recommendations to the Commandants and they passed orders to the German Magistrat.

The German administration was left unchanged by the Allied powers. The Magistrat of the City includes a Public Health Department headed by a Medical Officer of Health.

The City is divided into 20 districts or Bezirke each with a Burgomaster and its Health Department. These have not the power of a London Borough, as they come under the general control of the Magistrat and do not raise a separate rate.

I would remind you that the City had capitulated to the Red Army on May 2, consequently the German Officers at the Magistrat and the districts on our entry were holding posts with Russian consent.

Of the six districts we took over, all Medical Officers of Health, except one, had been appointed, not for their ability but for their political views: suffice it to say that one was not even a medical man and another had "done time" for illegal operations. Drastic action was immediately taken and one month after British Military Government was established efficient medical officers were in each district of the British Sector.

Although British troops moved in on July 4 British Military Government did not take over its sector till July 12, 1945. During this time one found certain conditions, namely: (1) Polluted water supply. (2) Sewage system—20% going into sewage works only. 80% flowing into rivers and canals in the centre of the city. (3) Major epidemics of dysentery. (4) Shortage of medical supplies, some large hospitals having as little as one pint of ether and no sulphonamide. (5) Inadequate food supplies, no salt, and ration cards not being honoured. (6) High V.D. rate. (7) Major fly nuisance. (8) Shortage of hospital beds, 5,000 for the area, 50% of which were unfit for use in rain or cold.

These conditions applied to the city as a whole and should obviously be treated by uniform measures. These uniform measures should have been taken by agreement of the Allied Public Health Committee. (At the end of August the French took over a portion of the British Sector, and the committee then became quadruplicate.)

The hospital problem gave us great concern. As already mentioned, we had some 5,000 beds in our area, all the hospitals being damaged to a major degree. To increase the number of beds, repairs had to be pushed forward and other new buildings utilized by repairs and conversions. With the great help of the R.E.s attached to Military Government a special German Labour Force was brought in from the Zone and hospitals were put on No. 1 repair priority. The difficulties were many but were overcome; for example, glass was just not available. We found, however, that the Central Store of X-ray Films of the Insurance Organization of Germany was housed in Berlin in the British Sector and practically undamaged. Although these were valuable records I considered it more important to have them cleaned and use them instead of glass. These were used, but before we could utilize them we had to fly in nails as there were no nails in the city. It is interesting to record that every hospital of any size had a deep operating theatre block and beds for 6 or 7 patients, and in no instance did we find one of these deep units damaged by bombs. The Germans had in Berlin large surface air-raid shelters (bunkers). These could house some thousands of people, they were 4- to 5-storey sary interference by occupying powers are able to cope with any emergency that may arise. In my opinion the Germans are quite capable of re-establishing their Medical Services without large numbers of British personnel supervising their activities.

Dr. H. A. Raeburn (*late Lieut.-Colonel R.A.M.C.*): Colonel Kennedy has dealt with the varying situations met in Germany from the time British troops first crossed the Rhine. Dr. Horsbrugh has described the special political circumstances in Berlin—emphasizing the chaos and malnutrition. I will try to say something on another general matter—that of refugees—and refer to some of the more strictly medical problems, but before doing so I cannot resist mentioning one lesson driven home during our time in Berlin—the basic importance of environmental hygiene. In the early days even an increasing tuberculosis rate seemed of rather academic interest compared with faulty water mains and sewers.

The large-scale movements of population which followed the end of hostilities have already been mentioned by Brigadier Kennedy. In Berlin there were few displaced persons but the problem of the German refugees soon became acute.

You will already have appreciated that Berlin was rather like an island in a Russian sea. For practical purposes all refugees came from the East—the Russian Zone of Germany, and ceded territory—and were made up of three classes. A few were Berlin residents returning, and Germans evacuated from the West on their way home, but the vast majority were the inhabitants of the ceded territories. In theory there was some sort of agreement on the orderly evacuation of the refugees, but as far as Berlin was concerned, they seemed to arrive in the most haphazard fashion. Another theory was that refugees were not permitted to enter Berlin at all, but in practice, in October and November, they came at the rate of 20,000 per day. The difficulties can be imagined when I say that one temporary camp set up for 1,500 refugees had to accommodate 8,000. I suppose these people found themselves in a countryside where food and shelter were lacking, and the natural tendency was to make for a big city where, in their utter misery, they might expect some help. Most roads and railways from the eastern provinces passed through Berlin, and a common sight during the autumn of 1945 was crowds of refugees leaving the railway stations and coming from the eastern part of the city into our sector. The lucky ones were pulling their belongings along in carts, the more unfortunate carrying them on their back. They arrived by train and on foot. Trains were crammed and at one station in one month 100 dead bodies were found on arrival. Many had had little food for a number of days and had been subject to much maltreatment. One particularly troublesome condition was lacerated feet, which were slow in healing in the debilitated people.

One particular incident sticks in one's memory. One evening we heard that a barge with 200 children had arrived. They were a Lutheran children's home from Stettin, who had been suddenly turned out of their premises. For want of anything better they moved to a barge which for lack of any other place to go came to Berlin. The children had hardly any food for the three weeks' journey and they had to be kept in bed in the holds as there was no level deck; 5 died of starvation. The nursing sisters did a fine job and everything was spotlessly clean. One did not have to be very sentimental to be touched by the way the children were kept occupied by singing some of the very charming North German folk songs. We managed to put this home into a school in Berlin. The person who was most relieved to see the children fixed up was the barge skipper, who I think was afraid he might be pressed into service as a children's nurse. With better feeding they soon improved although 20 had to be admitted to hospital and they ultimately went to the British Zone.

It was found, however, that this dispensing of prescriptions for private practitioners' cases led to black-market selling of British drugs and had to be stopped. Active measures were taken to get chemists' shops supplied through the normal trade channels, for use of practitioners.

What of feeding the city? On taking over Military Government, Britain also took on the responsibility of feeding the civilian population in their own sector. It was agreed that all foodstuffs should be brought to a central depot and distributed through the Magistrat. This was done because only certain foods were available from certain Zones. No agreement could be made for the normal larder of the city to be used as this was in the Russian Zone.

In order to bring in her quota of food Britain had to transport this some hundreds of miles on a far from efficient rail system.

The early days of occupation left the German people very short of food. In theory the following rations were available to the people:

Heavy workers	2,443 Calories	Children under 15	1,500 Calories
Workers..	1,957 Calories	Non-workers (including housewives, expectant mothers) ..	1,200 Calories
Sedentary workers	1,581 Calories		

In the early days, ration cards were seldom honoured to the amount allowed. Germans employed in the offices of Military Government were on No. 2, i.e. 1,957, but the amount they obtained was probably less than 1,000. One found in our own office girls fainting at the desks and the ones that carried on were in such a poor state of health that little concentration for work was possible in the afternoons. Their state of health was so bad we had to give them a midday meal in order to get the work out of them. The meal was roughly 300 calories.

The No. 5 class (1,200) was called the "death class". This was very true where it was the only source of food. For example, in the prisons all prisoners were on No. 5 rations. These were, in fact, getting less than 1,000. The prisoners were in such a state that no hard labour was carried out. Hunger œdema was rife. Prisoners who got to the stage of hunger œdema did not last more than one or two weeks before they died. No adequate diet was available in the prison, or, in fact, in the general hospitals for the treatment of the prisoner with hunger œdema.

Rations for the population were seldom up to date in July, August and September. We were for two months without fat rations. In September, a British Nutritional Team visited the city and reported that the nutritional state of the people of Berlin was the worst in the British occupied area of Germany.

The Public Health Section recommended in the early stages that No. 5 ration should be abandoned. This was eventually adopted, first in the prisons and then for the population as a whole. The amount of black-market food available was small and at such a price (£20 for one kilogram of butter) that it was not a factor in the general health of the population.

Six months after the occupation by the British, all ration cards were regularly honoured and the general state of health of the Berliner so improved that the winter did not cause the anxiety which was feared. We went through the winter without undue major epidemics.

The rations after six months had been increased for the class 4 children (1,300 to 1,500 Cals. + milk) and class 5 ration increased to 1,500 Cals. and these were being honoured. Hospital patients and expectant mothers got ½ litre milk *per diem*. Additions of cod-liver oil were issued to children under 5 years. One can say that Berlin was the worst-fed area in the British Zone in July and was probably the best-fed at the beginning of 1946 as they did not suffer the cuts in the rations this year that occurred in the other parts of the British Zone.

In conclusion may I say that in my opinion the German Medical Services in Berlin were adequate and efficient when I left in April, and if left without unnecesspoke with a number of German clinicians and I think it must be agreed that some people, incubating the disease, were killed by this measure. One physician made a curious observation that the disease itself seemed to be as severe in the inoculated, but that complications were less frequent. It must be emphasized that large numbers of refugees were expected, and that benefits ought to show themselves in the spring and summer of 1946. In actual fact, enteric has been much lower this summer—the average was 50 cases per week.

Typhus.—Control of typhus was, I think, a triumph of preventive medicine. Apart from the fact that Germany's surrender took place in the summer, the stage seemed to be set for an epidemic. No epidemic occurred, although there were some 284 cases in the city (37 in the British Sector), for the six months July 1945 to January 1946. The first cases appeared in August and there was a considerable number by the end of October. I had an opportunity of seeing practically all the cases in the British Sector and a considerable number in other sectors. So far as one could determine, all cases in the British Sector, with one exception, were infected elsewhere. The exception is of interest. This case occurred in a nurse who had received anti-typhus inoculations with the mouse lung vaccine. This vaccine was subsequently withdrawn as it was found to be ineffective.

The control depended essentially on the louse control of refugees. The necessary equipment and supplies were obtained from British sources and a British Hygiene Section in Berlin supplied N.C.O. instructors, who trained German personnel. Mass dusting of the whole population was not considered necessary as the German is naturally clean. Anti-typhus inoculation was given to doctors, nurses and others connected with the sick and refugees. Clinically, rashes were not marked, the "typhoid state" and lineal injection of the conjunctiva being the most striking symptoms.

Venereal disease.—This problem was of special importance owing to the high incidence among British troops. Conditions were ideal for its spread. There had been the usual wartime increase. With the fall of the city, administration had broken down and there was separation of families, often without news of each other and the city was full of refugees and foreign troops. Destitution and prostitution were rife. One officer summed up the situation somewhat cynically with the remark: "Few morals could withstand a tin of sardines." It is certainly true that many women were driven to prostitution owing to lack of food and the disease was found in all grades of society. Coupled with this there were inadequate treatment facilities, sulphonamide being especially short.

One cannot give the incidence with any certainty. In one district a survey revealed that 10% of women between the ages of 15 and 45 admitted suspicious symptoms. The Berlin M.O. put the figure as high as 40% of the female population.

The measures taken were designed to trace infected women and improve treatment. As you may know, when a British soldier is infected, he is asked to supply particulars of the possible source. Women infecting Allied troops were detained until free from infection, a special hospital being set apart for this purpose. When this work got properly organized, some 80 to 90% of reported contacts were traced. It says much for the versatility of the British "other rank" when I tell you that this job of tracing contacts was organized by two Military Police N.C.O.s—one an East End hawker and the other a goods porter from near Bristol. Their jeep, very much overloaded with persons being brought in for examination, was one of the sights of Berlin.

A variation was the raid on the black spot. Berlin has its notorious cafés like any other city, and scrutiny of confidential reports revealed where "picking up" was taking place. Briefly, the café or area was surrounded by the German police

It was impossible to patrol the city boundary effectively and I think it must be said that the Russians who controlled the eastern part of the city seemed to show very little interest in the matter, their attitude being "the Red Army has forbidden any refugees to enter, therefore there are none".

When faced with such misery, the British reaction is to do something, even though by doing so the difficulties were increased as more refugees were attracted. Soon the number of refugees in the British sector was much greater than in the rest of the city. Camps were set up by the "Refugee and Displaced Persons Section of Military Government" and the luckier refugees found accommodation there. The stream died down by the end of the year and by that time we had a more or less permanent camp with adequate accommodation for 10,000 persons.

At the peak it was a bit of a mystery where the majority of the refugees went. They seemed to find accommodation in cellars and only appeared when there was a possibility of their being evacuated to the British Zone in the West. It was realized that Berlin might become a plague spot, and arrangements had to be instituted to prevent infection spreading West. Before evacuation, refugees had a medical examination to assess fitness for travel, and a quick inspection before boarding trains or buses to eliminate infectious disease; they were deloused with D.D.T. and these measures were effective.

Another interesting movement was the return of German prisoners of war from the East. Their transport was the responsibility of the British Military Authorities but we had to arrange for a hospital for the reception of their sick. Sepsis due to undressed wounds caused most of the admissions. What one remembers of this hospital is the all-pervading smell of pus. It made one realize what Medicine owes to Lister.

It is against such a background that the question of epidemic disease has to be considered. Dysentery was the chief disease met with on arrival and in July 1945 there were some 2,000 notifications per week. The insanitary conditions of the city gave every opportunity of spread. It was impossible to do complete bacteriological examination of all cases but the few German laboratories working found that the disease was largely of the Flexner type. Of interest is the high fatality rate, 28%, which could be attributed to the general debility of the population, the lack of suitable drugs and the impossibility of dieting. Some cases seemed just to die. Pathologists reported that at a post-mortem they could recover the organism, but the bowel showed no inflammatory reaction: the patient had no power to resist.

Enteric was the disease which caused most anxiety. On our arrival in July it was known this disease was occurring—some 70 cases per week—but in the latter part of August the situation became alarming, the number of notifications reaching over 700 a week—mostly true typhoid. This rise coincided with an influx of refugees from Eastern Europe and it was estimated that 80% of the cases were imported. Hospitals were crowded and many cases had to be treated in unsatisfactory homes. In all, 12,700 cases with a fatality rate of 12% occurred in the city from July 1945 to January 1946. From the remarks on refugees you will have gathered we had no official information about conditions in the areas from which the refugees came—if rumours could be believed many villages were immobilized by the disease and cases were left lying in the street: also we had no control until the refugees arrived in the British Sector. In view of this, the drastic measure of compulsory inoculation was ordered and completed towards the end of September. The stamping of ration cards used by the Germans afforded an easy method of ensuring that people were inoculated and in actual practice over 90% of the population were immunized. One German M.O.H. asserted that inoculation was voluntary but people would get no food unless their cards were stamped!

One keeps an open mind as to the efficacy of this measure. It is true that the epidemic declined, but there would have been a seasonal decline in any case. One

Section of Otology

President—H. V. Forster, M.C., M.B., Ch.B., M.Sc.

[*November* 1, 1946]

Otology in School Children and Child Welfare

PRESIDENT'S ADDRESS

By H. V. Forster, M.C., M.B., Ch.B., M.Sc.

Those about to undertake the practice of Otology at the request of a local Education Authority will find special interest in the work of the late Dr. Kerr Love (1919) a Past President of this Section. This is a record of three years' work in the treatment of ear disease undertaken for the Glasgow School Board between the years 1912 and 1915. It is, to quote the author's words: "Essentially an essay on the Prevention of Deafness. Before the ink is well dried on its pages a Ministry of Health may be at work and it is the writer's wish that the progress of the new service will be such as soon to render the teaching of the book out of date.

Kerr Love was also asked for his advice on the treatment of ear disease in the schools under the control of the Secondary Education Committee of the county of Dumbarton, though the chief object of the Committee was to have cases of tonsils and adenoids treated by operation. My own work in Lancashire in the year 1919 was also started by a request to perform these operations and many others, no doubt, have had the same experience. We all have probably given the same answer, namely that we should be offered facilities to examine the candidates for such operations and discuss their indications, at the same time recording our observations on the condition of the ears, nose and throat.

I was well aware at the time that many operations were being done in this country upon the palatine and respiratory tonsils of school children for which the Ministry of Education had already granted certain facilities. Alison Glover (1938, *Proc. R. Soc. Med.*, 31, 1219) reminds us that the number of tonsillectomies officially recorded in public elementary school children for the year 1919 were for London, 11,817 and for England and Wales, 42,004.

Has this development in the practice of otolaryngology in school children gone far enough? Has ear disease been satisfactorily treated in the young?

A world war has descended upon us again laying bare the defects in our armour. The medical boards of the Ministry of Labour and National Service have been and still are busy examining the youth of the country and send to the otologist for his opinion the many cases of ear disease so often unconsciously tolerated and neglected by these young people no longer under the care of a school medical service.

Professor Canfield of Harvard (1945) showed an admirable colour film of the management of consultations in otolaryngology in a children's clinic in America. That, to me, was an example of how the work should be arranged. In my own, and the women who could not give an account of themselves or were known to the criminal police were detained and examined by the German Health Department. From September 1945 to January 1946 some 900 women were rounded up. Over a quarter were found to be suffering from venereal disease. In this way a considerable number of professional prostitutes were brought for treatment, though we probably did not find the respectable person forced into prostitution by destitution.

The next step was to try and improve treatment facilities. The German venereal disease scheme depends on the use of private physicians rather than public clinics. There was a great shortage of sulphonamide and arsenicals, but, sufficient supplies were obtained from British sources. These, however, did not completely solve the difficulty as sulphonamide had enormous value in the black market, 5s. to 7s. 6d. per tablet. It was felt that British drugs in such circumstances could not be handed out *ad lib.* We therefore got the German M.O.H.s to nominate doctors for each Bezirk and drugs were issued and accounted for by the number of cases treated. There was much inadequate treatment by black-market drugs, leading to sulphonamide-resistant cases.

Early this year, penicillin was made available in limited quantities for the treatment of persistent cases who had infected British troops. The venereal disease specialists in the British Military Hospitals trained German physicians in its use and a special hospital was set apart for this treatment, with satisfactory results. I must say that this penicillin caused us, as doctors, some heart-burning, as we had to limit its use to venereal cases, and to refuse it when it might have saved life.

Tuberculosis.—Being essentially a social disease, it is not surprising that the incidence of tuberculosis increased. Statistics were particularly difficult to obtain, but as far as we could find out the incidence per hundred thousand per annum had increased from 25·8 in 1938 to 48·9 for the six months July 1945 to January 1946. It was probably much higher. The tuberculosis question was early raised at the Kommandatura, but nothing much was decided. I hope you will not think us unappreciative of the tragedy of tuberculosis when I say that in the early months we thought the discussions rather academic; it seemed more important to concentrate on straightening out the general chaos and improving nutrition rather than to think of tuberculosis alone. Another point was, that little could be done. We did get some slight additions to the diet of the tuberculosis patient but the question of accommodation was difficult. Like other cities, Berlin's tuberculosis accommodation was largely outside the city. Travel difficulties made it impossible to send any patients to sanatoria in the British and American Zones in the West. A number of individual cases had travelled—or rather they were issued at our recommendation with travel permits. Frankly, we never knew what happened to them and one had an anxious feeling that giving a recommendation merely absolved one from the odium of doing nothing.

There was a large tuberculosis colony on the outskirts of the city in the Russian Zone of Germany, in use by the Red Cross. Our Russian opposite number did his best to recover some accommodation but could get no concession from his H.Q. The most we could do was to see that existing accommodation was used to the best advantage and improvise a few additional beds. I am glad to say that regular arrangements for the use of sanatoria in the West have been made.

Maternity and child welfare.—The Berlin set-up was essentially the same as our own. It so happened that the clinic buildings were usable and as most of the doctors were women the regular staff were available. Activities were handicapped by lack of supplies, but valuable educational work was done in instructing mothers in the best use of available food. The tragic infantile mortality reached of some 250 per thousand per annum might otherwise have been higher.

with its proper ventilation though moderate enlargement may not. We know that acute tonsillitis as part of an acute inflammation of the pharyngeal lining is sometimes associated with acute otitis media. Perhaps I am concerned with the fear that indiscriminate removal will do harm.

I do not like the term chronic tonsillitis for it may be argued biologically that it is a normal process but there will be no disagreement that removal of the palatine tonsil regardless of its size cures that disease named most suitably by Continental writers—"tonsillitis with free intervals" and with brilliant results in the health of the child.

The examination of the nasopharynx in children is difficult but a trial with the post-nasal mirror in every case gives excellent practice and many successes and I have given up long ago the digital examination of the post-nasal space in children except under general anæsthesia.

It will be agreed that in infections of the middle ear and interference with its proper ventilation, the hypertrophied and diseased respiratory tonsil of Luscha should be removed surgically. There are, however, numerous conditions within the nasal passages of children which do not benefit materially from this operation and one of these is allergic or vasomotor rhinitis which is by no means uncommon. It is sometimes associated with secretory otitis.

Some years ago Proetz (1931) described acute allergic middle-ear attacks difficult to distinguish from the early stage of acute suppurative otitis media and Koch (1946) recently published a cytological study of middle-ear secretions in which he discusses the so-called eosinophil chronic otites. There has been a call to our British Association of Oto-Laryngologists for closer co-operation between the pædiatricians and ourselves. I should especially welcome their help in the solution of the problem of the so-called catarrhs including catarrhal middle-ear deafness which is not to be dismissed as one of essential Eustachian obstruction.

Blegvad (1931) once asked the question: "Is it necessary to maintain as an independent malady the occlusion of the Eustachian tube?" a question discussed later by Holmgren (1931) when describing his experimental research on its function. War has added interest to the problem because of aviation pressure deafness, a subject which has been introduced here by Simpson and discussed in detail by McGibbon (1942) and I understand that treatment by radiation has now been used to relieve it. I have no experience of radium or radon therapy as applied to the nasopharynx in the middle-ear deafness of children in the manner of Crowe and Guild (1938). The well-tried manœuvre of inflation by Politzer's method gives brilliant if temporary relief in catarrhal otitis. Gone for a while is the depression of the drumhead and that strange grey translucent picture lightly coloured by a pink reflex from the tympanic wall. Some children are remarkably courageous to inflation but others are alarmed, perhaps there are members here to-day with memories of this experience in their own childhood and I have already remarked how fortunate we are that Nature alone does so much to relieve the growing child of his disability, but now and again we meet a striking case of the resistant Eustachian tube. I have in mind a boy of 7 years, his right ear successfully ventilated by Politzer's method in November 1930, but later without success. In January 1939 he retired at last from the unequal contest which had included several insertions of the Weber Leil intratympanic tube and one temporarily successful paracentesis. During those years, reluctantly disturbing the peace of his school holidays I had repeatedly observed a collection of fluid in his middle ear. Such difficulties recall to me a discussion opened here by Mollison (1934).

A depressing variety of middle-ear deafness is one where, in spite of rational medical and surgical treatment to the nose and nasopharynx the child remains examinations are made in the presence of the parent or some responsible deputy who is questioned in simple language about the child's complaints. In one clinic the school medical officer is also present. The form originally designed by Kerr Love makes a useful case sheet and, when completed, a permanent record to be filed and consulted again.

In their examination and treatment, the diseases of the outer ear do not call for special comment. But certain difficulties of management arise, as, for example, the case of keratosis obturans by no means uncommon in children. The study of the disturbances of the epithelial lining of the external auditory canal is our particular field of dermatology, but it is of importance also to us as surgeons for it leads to a better understanding of the behaviour of the epithelial covering which we hope will invade our operation cavities, those cavities of the hindmost end of the middle-ear cleft laid open by radical or modified radical operations in the surgical treatment of chronic suppurative disease.

THE PREVENTION OF DEAFNESS

In the prevention of deafness it is fortunate that syphilis in the future parent is better treated nowadays and we begin to understand how german measles infecting the pregnant mother may damage the auditory organ in the fœtus, but until the problem of the early development of otosclerosis has been solved it is in the treatment of suppuration and the so-called catarrhal conditions of the middle-ear system where so much can be done for the young.

In case-taking one finds many parents are deaf and in suppurative middle-ear disease I have seen repeatedly quite striking examples of a hereditary tendency.

There is some encouragement from the intermittent nature of childhood deafness, because we feel more hopeful of eventual recovery. Mother Nature, unaided, can do so much or we should find the hard of hearing more often in the adult population. Some years ago in Esthonia, E. Sarreste (1935) carried out researches in 1,366 pupils of schools in the city of Tartu. The ages varied from 7 to 20 years. He concluded that catarrhal otitis media diminishes with the age of the pupils and in the majority of children over 13 years of age there is less and less hope of improving the hearing. whereas below 13 years the greater number get well either spontaneously or as a result of rational treatment.

It is obvious that we must examine with specialist thoroughness the oropharynx, nose and post-nasal space and at once we are brought face to face with the tonsil problem.

Of the exact physiological significance of the palatine tonsils we remain uncertain. Schlemmer has insisted that they are an integral part of the pharyngeal lining and serve no separate functions. Glimstedt showed how the so-called germ centres, absent at birth, develop thereafter as a reaction to invasion from the outside world, and to Grossmann and Waldapfel (1926) we owe an understanding of what goes on in these centres during acute tonsillitis. Policed as they are during health by mononuclear cells, they are entered in times of acute bacterial invasion by the polymorphonuclear leucocyte in the pursuit of organisms. To destroy these organisms or prevent their development we now have the assistance of the sulpha group of drugs but on the other hand we know that they may curtail the recruitment of the granular leucocyte.

Torsten Skoog (1936) provides an attractive answer suggesting the theory that the lymphadenoid tissue of the pharynx has a sensitizing effect on the reticulo-endothelial system of the body.

What I should like to know is to what extent the palatine tonsil influences the health of the middle-ear cleft. Considerable hypertrophy presumably interferes

The child's ear provides special opportunity to observe the progress of moist defects of the membrana flaccida and the dry crusts which form in this area and to speculate, not without anxiety, what changes are taking place beneath them . . . I remember a publication by Marcus Diamant (1937). He believed that the otitic origin of cholesteatoma had not yet been proved and the title of his paper is in the form of a brief but significant question: "Acute or Chronic Otitis?"

What kind of major operation should be done to drain the middle-ear system in children to treat disease inaccessible to conservative measures?

I prefer to be kind to the tympanic contents after laying wide open the attic, aditus, the mastoid antrum and the attendant cellular system. One hopes thereby to retain more of the hearing function, but the tympanic lining has considerable powers of recovery whereas the parts behind invaded in due time by a foreign covering of squamous epithelium are subject to changes of complexion. Might I be allowed to suggest that the younger otologist will be saved much wounding of his *amour-propre* by remembering that squamous epithelium lies uneasily upon bone.

Very occasionally I have performed completely radical mastoid operations on both ears in the child and I think of one, now grown up, who has given useful service to her country in the A.T.S., though how this enthusiastic volunteer managed to slip through the net of medical inspection nowadays I cannot say.

What of the after-treatment of the mastoid operation for chronic middle-ear disease in children? I prefer to cut a Ballance's flap of the soft meatal tube but would not cross swords with those of my colleagues who prefer to leave it uncut. A lightly filled rubber finger-stall is inserted and later removed with little pain to a child. The late Sir James Dundas-Grant thought well of this method.

When dressings have been removed the ear is washed out once or twice daily with weak eusol and later with the mercurial lotion which serves well after discharge from hospital. I am not depressed by some temporary filling of the cavity by nature in the healing process.

Granulations of the meatus react well to the chromic acid bead and in time a layer of some depth recedes leaving epithelium on a hard seat. The child is now made safe, his general health improves remarkably and his morale has not been depressed by treatment of the ear with gauze packing.

In reading this Address I am aware that its teaching is elementary though supported inevitably by some experience provided by the passing of time, but we who practise medicine and surgery in this country are on the eve of great events. Our rulers are busy planning a comprehensive medical service for the nation and the problem of deafness has aroused fresh interest in high places. To help solve it we must begin with the child. I have no doubt that appeals by the otologist to develop his work for the children of the nation will be received with sympathy and that means will be provided to assure that it is well done.

REFERENCES

BLEGVAD, N. RH. (1931) *Acta Oto-Laryng.*, 16, *fasc.* 2-3.
CANFIELD, N. (1945) *Proc. R. Soc. Med.*, 38, 628. Film, "The Right to Hear" (State University of Iowa).
CROWE, S. J., and GUILD, S. R. (1938) *Acta Oto-Laryng.*, 26, *fasc.* 2.
DIAMANT, M. (1937) *Acta Oto-Laryng.*, 25, *fasc.* 6.
GROSSMANN, B., and WALDAPFEL, R. (1926) *Acta Oto-Laryng.*, 10, *fasc.* 1.
HOLMGREN, G. (1931) *Acta Oto-Laryng.*, 16, *fasc.* 2-3.
KOCH, H. (1946) *Acta Oto-Laryng.*, 34, *fasc.* 4.
LOVE, J. KERR, (1919) Diseases of the Ear in School Children. London.
MOLLISON, W. M. (1934) *Proc. R. Soc. Med.*, 27, 1069; (1945) 38, 418.
PROETZ, A. W. (1931) *Ann. Otol. Rhin. Laryng.*, 40, 74.
SARRESTE, E. (1935) *Acta Oto-Laryng.*, 22, *fasc.* 4.
SIMPSON, J. F., MCGIBBON, J. E. G., *et al.* (1942) *Proc. R. Soc. Med.*, 35, 245.
SKOOG, TORSTEN (1936) *Acta Oto-Laryng.*, 23, *fasc.* 1.

deaf. The middle ear ventilates well and one cannot recognize through the drumhead any retained secretions or visible signs of adhesive processes. I am reminded, however, that the late Sir William Milligan speaking some years ago in this room expressed the opinion that the round window, placed as it is rather low in the tympanic wall is more readily exposed to pathological disturbances which eventually curtail its resilience.

SUPPURATIVE OTITIS MEDIA

In the treatment of acute suppurative otitis media we have had the opportunity at these meetings to discuss those newer aids, the sulpha group of drugs and penicillin.

If more children suffering from acute otitis were admitted to hospital and there had the assistance and proper control of the new therapeutics, no doubt the incidence of chronic suppuration would fall.

At the school clinic, however, it is most satisfactory to see so many discharging ears dry up and heal under simple conservative treatment, by which I mean irrigation with a suitable mercurial lotion followed by the instillation of alcohol drops and the pursuit of granulations with the chromic acid bead.

Lotion for Syringing:

℞	Mercuric chloride ..	4·375 gr.	(0·2838 g.)
	Sodium chloride ..	4·375 gr.	(0.2838 g.)
	Methyl violet	0·01 gr.	(0·00065 g.)
	Aq ad	℥ x	(300·0 c.c.)

Sig. A tablespoonful to be mixed with three tablespoonfuls of warm water and used for syringing out the affected ear.

See Solvellæ Hydrargyri Perchloridi in B.P.C. 1923, p. 1435, which gives methyl violet. I prefer this to the methylene blue of the later edition. The liquid is dispensed to avoid the danger of keeping mercurial tablets in the home.

Spirit Drops:

℞	Acid Boric	10 gr.
	60% Alcohol	℥ I

Sig. Half a dozen drops to be run into the affected ear after washing out and drying with a cotton-wool mop. Repeat the drops later in the day after mopping out only.

I do not wish to raise a controversy about the relative merits of the wet and the dry treatment. I find syringing in the hands of the school and child welfare nurses eminently practical so long as they have the encouragement of parents and teachers in the regular attendance of the child.

The ætiology of much chronic suppurative middle-ear disease is rather mysterious. We know how responsible are the acute infections and of the exanthemata Kerr Love gave first place to measles but some cases develop in a strange manner especially in the attic region and we have the problem of cholesteatoma. Childhood naturally provides the most useful period in which to study them.

I should like to say a little about those cases selected for operation though not all of attic type. What I call the "black" mastoid is often seen. The cortex being carefully removed we notice at once a dark reflex which suggests the proximity of the lateral sinus, but proves to be the first of a widely disposed system of cells filled with a mucoid-like substance and lined by a darkly stained membrane. I should like to know what happens to the mastoid system of such children who have avoided operation and perhaps disaster well into adult life. Might these cells be crowded out eventually by dense bone as far as the antrum?

In operations for attic disease we may find in children unsuspected cholesteatomatous deposits filling the cells right down to the tip of the mastoid process.

I should like to be better informed about the subject of cholesteatoma and the strange behaviour of the epithelium at the circumference of the tympanic ring.

Mr. J. F. Simpson exhibited some radon seed applicators which he had had made according to measurements provided by Major Fowler of the U.S. Air Force. These he had used in a very short series of cases. The small capsules, which he exhibited, unscrewed and took a radon seed (75 millicuries). Both were put in the nose at the same time, after spraying with cocaine. They were rested against the orifice of the Eustachian tube, the handles crossed at the anterior nares and tethered with a little piece of rubber band so as to bring them into contact with the Eustachian orifice. It was calculated that at a depth of 0·5 cm. from the wall of the capsule they would deliver a dose of the order of 750 r at each application. All these calculations had been made by the radiophysicist at St. Mary's. It was very necessary in all this work to have the help of a radiotherapist. When using radon seeds allowance must be made in calculating the time of application for the gradual decline in activity of the radiation. The usual dosage, if the seed was fresh, was twenty-two minutes. The capsules were left in situ both together for this period and four such daily applications in succession constituted a course. More than one course was sometimes necessary and if the case required it one could wait two or three weeks—preferably three—before beginning another course.

Mr. Simpson thought the treatment especially suitable for children in whom catarrhal deafness persists after removal of tonsils and adenoids and in whom politzerization gives only temporary improvement.

Mr. Gavin Young said that there were two main types of patients in this category. One consisted of the patients who suffered from nasal allergy; very often these were only children, and they did not appear to benefit at all, or benefited only very little, from removal of tonsils and adenoids. The other consisted of patients with chronic antral disease. It might be that in the damp west of Scotland they met more of these cases than in the drier regions of the south, but certainly a considerable number of cases did not clear up because of chronic antral disease, and he felt that rhinology had failed so far to deal adequately with this subject by failing to elucidate the pathogenesis of the condition.

Miss Winifred Hall said that her interest in these cases had been rather from the sociological than the clinical side. She described the working of school children's clinics where the responsibility for treatment was divided among several people, and stressed the need for these children to be dealt with as hospital cases, where all ear, nose and throat conditions could be treated by the same surgeon, who would also have full use of the hospital's radiological and other facilities.

Mr. F. C. W. Capps said that otologists who were called on to advise upon the disposal of these children should also carry out the operative treatment, at any rate all major operations, and should have facilities to follow these children up afterwards. He was asked, about 1934, by the Chief Medical Officer of the L.C.C. to make a survey of the aural treatment of children in London. He found the aural clinics very scattered, quite isolated from hospitals, and often in church halls and other unsuitable places. When operations were required they were sent away to a hospital outside London and operations were performed sometimes by men of very little experience in aural surgery. Some results were very bad. Much of this was in process of alteration when the war broke out, and the otologists running these clinics were being attached to a proper L.C.C. hospital with all facilities and ancillary services. Here they carried out the operations themselves, and all the necessary follow-up was done. This arrangement, which had given much improved results, broke down owing to the war, but he hoped that it would be revived.

As to chronic antral infection, or, perhaps not always "infection"—sometimes there was a chronic thickening of the lining of the mucosa of the antrum which led to improper ventilation or possibly improper insulation—he believed that in a large number of cases a routine X-ray picture of the sinuses was desirable. This need only be one view, to show the antra—the ethmoids were not so important as the antral cavity. He had found, too, that X-rays yielded valuable information upon nasal obstruction by adenoids. A true profile with soft tissue exposure was used.

He was prepared to confirm the President's impression that some of the cases of recurrent otitis media were hereditary.

Mr. R. G. Macbeth suggested that although it was admirable in theory that an otologist should be in ultimate charge of the investigation of these children, it was perhaps impossible in practice for him to see all of them. He wondered whether there was not a place in the scheme for the school medical officer with special experience, possibly the D.L.O., to act as a filtration bed. Many routine cases could thus be dealt with, and those requiring the otologist selected. It would be a tragedy if otologists were able to do less than their duty to those children most needing help, because they were expected to see very large numbers.

Mr. E. D. D. Davis said that he was in full agreement with the President, Mr. Capps and Miss Hall that all these cases should be examined thoroughly by an otologist in a properly equipped clinic. The patients should be examined again by the surgeon who undertakes any operation.

Mr. Francis McGuckin said that they were all grateful for the President's provocative Address on a wide subject. There should be no such entity as tonsils and adenoids to be contracted out by local authorities. The otologist should have the review of the whole child, accompanied by a parent, preferably the mother. Too little note was taken of the historical contribution which could be made by the home doctor. It was time that the local authorities realized that the consultation and observation were just as important as—probably more important than—operative work. As far as was practicable, decisions should be taken by the surgeon who was to operate. His own preference would be that these services should form part of the hospital service rather than remain an isolated unit.

Some criticism of the term "catarrhal otitis" might be advantageous. There were several groups: (*a*) the accident of an acute otitis chiefly bacterial in type; (*b*) repeated acute otitis of varying severity, unilateral or bilateral, with satisfactory healing between attacks; (*c*) the otitic lesion which was chronic from the start; (*d*) recurrent negative pressure syndrome characterized by in-driven drum and a little retention fluid in the middle ear. In these cases the fluid was almost certainly not inflammatory and it was possible that it was no more than an accumulation of mucus not eliminated via the obstructed tube. A further group (*e*) was the permanent perforation syndrome with loss of protection from without and the failure of the air piston from within. In these cases the bigger the perforation the more frequent the otorrhœa, but the safer the nuisance.

In some of the aforesaid groups the mechanics and pathology were understood fairly well, but in others less well. Did the term "catarrhal otitis" really describe any definite group either in relation to pathology or simple mechanics? Did it cover a reasonable entity either in respect of the ear or the upper respiratory tract? Tonsils had little or no direct effect upon the ear, though acute diffuse infection involving the tonsils might spread to the ear, and anything producing great swelling of the palate might occlude the tube. The role of adenoids was fairly obvious.

He believed it was just as unscientific to hold the entity of Eustachian obstruction as of bile-duct or urethral obstruction, without regard to the specific mechanical cause. In the past he had said that he knew of four definite causes, and he was still seeking for more. These causes were (1) trauma, which might arise from unskilled surgery with damage to the torus and possibly from a fracture involving the muscular relations of the Eustachian tube (barotrauma with flutter valve obstruction might also be included); (2) neoplasms, simple or malignant; (3) œdema of the torus, secondary to inflamed lymphoid tissue attached perhaps to the posterior limb of the torus or secondary to a flow of pus over the cushion, e.g. antral suppuration with a deep uncinate gutter or a sphenoidal suppuration (in these cases the rounded tubal entry could be seen to be reduced to a mere slit); (4) adenoids, in which case the usual obstruction arose from the mere covering of the tubal torus by the adenoid tissue, but he had already mentioned another possibility. The obstruction might be an uncomplicated mechanical thing or, if the cause be infective, then the aural result might be a mixture of inefficient air exchange plus bacterial complication.

There was no time to cover adequately the ætiology of chronic otitis, but he did hold the view that many cases—perhaps a considerable proportion—were chronic from the start, and he believed it was time the Section had a further full-scale discussion on cholesteatoma, which might include keratosis and aural dermoid. It had been his ambition, as yet unfulfilled, to have all the infantile ears in three hospitals in Newcastle observed and noted each day. He believed that in this way they might learn a great deal about the possibilities of congenital attic cholesteatoma and perhaps of primary pseudocholesteatoma. They had still to solve the problem of the acute ear which was smelly from the start and also of the extensive damage which might be quite unadvertised in the presence of a sterile cholesteatoma.

The President had coined the epigram "Squamous epithelium lies uneasily upon bone". That he fully agreed with, but it might also be added that keratinizing squamous epithelium might lie quite easily in the middle-ear cleft until such time as an accident occurred. Nothing more than moisture was required to turn this innocent condition into something threatening and destructive. The accident might be a common cold with a mild otitis, a visit to the swimming baths, or some other slight incident, but he thought they must admit that many of these cases were rendered active by the mere use of an ear syringe or the instillation of ear drops.

The President had asked for information about radiotherapy in the post-nasal space. The speaker had tried this on a few occasions where other therapy seemed unsuitable. The numbers were insufficient to draw any conclusions, but he was prepared to be disappointed.

Mr. A. S. H. Walford said that from experience around Cambridge he did not think there was any difference in the incidence of adenoids as between children from town or country. The condition had nothing to do with environment. The ordinary country population certainly had just as much adenoids as the town. There was also a considerable proportion of these children who were really suffering from antral infection rather than infected tonsils and adenoids.

Section of Radiology

President—WHATELEY DAVIDSON, M.D., F.R.C.P., F.F.R.

[*November* 15, 1945]

DISCUSSION: THE X-RAY TREATMENT OF INFLAMMATORY DISEASES

Dr. Mary Cripps: *The effect of X-radiation on the eye from its clinical aspects.*—Following the successful treatment by X-radiation of herpes ophthalmicus in 30 cases, I tried it on other conditions. I found that it had a definite usefulness in certain categories of ophthalmic cases but that its sphere was limited. Briefly, the application of X-radiation (where the intra-ocular tension[1] is normal or subnormal) to minor lesions yielded good results within three to seven days. If, on the other hand, the inflammatory condition from injury or otherwise was severe and the tension on an average above normal, a larger dose and a longer time were required. The aggregate effect of X-radiations on ocular tissue in my experience raised intra-ocular tension for a period too long to give satisfactory results from the point of view of visual acuity. For instance, a case of cataract extraction suddenly developed an infarct of lung, accompanied by vomiting and followed by opening of the extraction wound. X-radiation healed the wound with a temporary increase of intra-ocular tension which lasted for a period of almost two years and then returned to normal, a period of raised tension too long for the preservation of useful vision, but which may point to the ability of X-radiation to upset the vascular equilibrium for this period. The return to normal of the raised tension showed that the eye had been through a period of unstable equilibrium after X-radiation.

Therefore, I was forced to the conclusion that X-radiation for the successful treatment of ocular lesions must be confined to the category of cases where the intra-ocular tension was not raised and the lesions minor (16 cases). But when

---

[1] Intra-ocular tension: *Normal tension*—On an average 33 mm.Hg Schiotz Tonometer, without weights; *Subnormal tension*—On an average *below* 33 mm.Hg Schiotz Tonometer, without weights.

More could be done to prevent catarrhal infections in school children. The young child during his first term at school lost three-quarters of it through bad colds. Such a child is a carrier and should not go to school during a cold, but the mother complains that in that event the child lost his dinner and his free milk. He thought there should be some form of isolation. If a roll is called any child who showed signs of a cold should be inspected, and, if the temperature was above 99° he should be sent home or isolated with other similar children.

The ventilation was important. It is stated that the temperature of the schoolroom should not be above 65°. A temperature above 65° meant that the ventilation was inadequate.

He had seen cases treated by radium and deep X-ray therapy in which burns had occurred and the mucosa never recovered its normal condition. Serious damage had been done without any benefit to the patient. He advised every otologist to be guided by a skilled radiotherapist.

Mr. R. Scott Stevenson said that as we knew very little about the remote results of radium in the tissues of children it was to be hoped that it would not be used indiscriminately nor without careful supervision by an expert on radiotherapy.

Mr. W. A. Mill emphasized the dangers of unregulated radium treatment.

Mr. A. M. Ross said that one point to which attention should be drawn was that general practitioners and the public were still not sufficiently alive to the dangers of ear trouble in children. The dangers tended now to be further masked by the tendency to give the sulphonamide drugs for earache without much discrimination.

Dr. J. Alison Glover said that the latest figures for public elementary school children in London for the incidence of running ears was 0·5%; the figure was some 9 times that when he first entered medicine, and all otologists were to be felicitated on so great a reduction. He was heartily in sympathy with those who had spoken about home conditions. These—and, of course, school conditions also—were most important factors in otitis. Perhaps school hygienic conditions were not quite so important as home conditions, but they were extremely important, and every improvement in school buildings and in the home was to be welcomed. Fortunately, the overcrowding necessitated by war conditions did not seem much to have affected the picture. For some reason or other the incidence of otitis, the mortality from rheumatic fever, and the incidence of the other streptococcal complications after measles and scarlet fever had all been going down recently.

Asked by a member whether it would help matters at all if otitis were to become a notifiable disease Dr. Glover said that he would rather doubt whether formal compulsory notification would be helpful.

The President, in replying, said that the question of "acute or chronic otitis" in relation to the origin of chronic middle-ear suppuration, led one to inquire into the difficult problem of how cholesteatoma originated.

Mr. Simpson had shown how the "cross-legged" method recommended by Fowler was used for his radon applicators so that the applicators would remain closely applied to the region of the Eustachian orifices. He himself had feared to use radiation in any form. After all, the pituitary was not very far away and though it was true it was shielded by bone, it was the key gland of the endocrine system and serious consequences might follow if it were disturbed.

Mr. Davis had suggested that the otologist was worthy of his hire. Those in authority could not neglect the problem of the prevention of deafness and that of the complications attendant on middle-ear suppuration. The otologist must also perform a certain number of operations on the lymphadenoid tissue of the throat.

Mr. Scott Stevenson also had uttered a warning about the use of radiation. Among other points raised was the general practitioner's over-use of the sulpha drugs, but nevertheless he would rely on the judgment and wide experience of the general practitioner in their administration, though warn him of cases of persistent deafness and latent mastoiditis which sometimes followed the abatement of acute symptoms.

Healing.—X-radiation promotes and accelerates the process of healing. It exerts its influence not only superficially but to a great depth. This property adds to its value in the healing of deep penetrating wounds.

Blood-counts taken before radiation and which show an increase in mononuclear leucocytes as a result of a specific inflammatory lesion show that, after radiation, as the inflammation subsides, there is a reduction in number, and a return to normal of these cells. An especially persisting increase arouses suspicion of involvement of the uninjured eye by sympathetic ophthalmia as a complication of deep penetrating wounds.

Fibrin grafts when applied to gaping wounds of the sclera appear to irritate the eye at first but after X-radiation the eye gradually settles down and excellent results follow. The graft eventually is indistinguishable from the surrounding sclera.

Speaking generally eyes with normal or subnormal intra-ocular tension derived most benefit from X-radiation. *Minor* lesions recovered completely in a short period of time, about three to seven days. Cases of greater severity required a longer time to recover and were apt to be disappointing except where intra-ocular tension was subnormal. Eyes showing increased intra-ocular tension accompanied by pain from mechanical causes, e.g. glaucoma, do not derive much benefit from X-rays. The properties of X-rays associated with their action in depth prevent or abort sympathetic ophthalmia in the uninjured eye.

CONCLUSIONS

X-radiation for the successful treatment of ocular lesions must be confined to the category of cases where the intra-ocular tension is not raised and the lesions are of a minor character. When X-radiation was combined with ultra-short-wave diathermy satisfactory results were obtained (198 cases). Lesions healed with a minimum of scar tissue, intra-ocular tension remained normal and the maximum amount of visual acuity was obtained. Further there were no clinical signs of the disturbance of vascular equilibrium.

Dr. Alfreda H. Baker: *X-ray treatment of osteomyelitis of the fingers.*—One of the most troublesome complications of a septic finger is a persistent subacute or chronic osteomyelitis of one or more phalanges or of the metacarpus. The patient may be disabled for weeks or even for months after the acute inflammation has subsided by a persistent discharging sinus and by pain and tenderness of the finger. Permanent disability is not rare, and, if the digit involved is the thumb or index finger, loss of occupation may result. If, on the other hand, sound healing of the bone can be secured, the prospect of obtaining a useful finger is greatly increased. Too often, in an effort to cut short the infective process, the patient is subjected to several operations at which fragments of bone are removed under the misapprehension that they are sequestra and that their presence is delaying healing. Sequestra do form in some cases, and the loss of bone seriously deforms the affected finger. More often the friable, but living, decalcified bone breaks up under the persuasion of a metal instrument and fragments are pulled out. Even without the aid of X-ray therapy the bone may recalcify if left alone. Every experienced casualty officer learns in time the value of conservative treatment. The process may, however, be long and tedious, and the impatience of doctor and patient may suggest amputation as the quickest way to end the pain and to get the patient back to work. A method that is likely to promote complete healing and functional recovery in a matter of weeks is obviously worthy of attention. Such a method is combined with ultra-short-wave diathermy I obtained satisfactory results (198 cases). The equilibrium remained stable and the intra-ocular tension normal and there were no unsatisfactory sequelæ.

Technique and dose.—The apparatus used in treatment was the superficial X-ray therapy unit with a Victor's tube 100 kV. 1 mm. Al. inherent filter equivalent 5 mA. 27 cm. focal skin distance. *Dose*: The doses used by Dr. Dalton and later by Dr. Woodham of the Ipswich and E. Suffolk General Hospital are as mentioned hereafter. All are expressed as surface/r. Time taken to deliver 100 s/r 1 min., 18 sec.; 50 s/r 39 sec.

Dividing the cases according to ophthalmological signs and symptoms into acute inflammatory (or traumatic) cases, and chronic cases, the optimum dose used for the acute variety was 200 to 225 r given as 100:50:50 r *or* 75:75:75 r. The interval elapsing between each exposure was three to six days. The whole treatment was given within ten to fourteen days.

Ophthalmologically chronic cases.—These reacted better to smaller doses, so the optimum total employed was 125 to 175 r spread over three weeks, as follows: 50:50:25 r *or* 75:50:50 r. The interval allowed between each exposure averaged seven to ten days, the whole treatment having been given in three weeks.

Action.—Evidence of reaction to X-radiation may be deduced from the hyperæmia of the ocular tissues. Whether the value of X-ray depends on the direct effect of radiation on the pathological cell which is more sensitive than the normal one, or whether it is due to the stimulating action it exerts on the neighbouring tissue is not determined. Probably all these various factors operate together but each with varying intensity in individual instances.

The effect on ocular tissues.—The conjunctiva is the most sensitive of all the ocular tissues to X-radiation. The lens appears fairly resistant but when exposed to too heavy radiations may become cataractous. Corneal ulceration and interstitial keratitis have been described after prolonged exposure to X-rays. The retina offers a fair degree of resistance. The action of X-rays on vitreous which has prolapsed is interesting. After X-radiation the vitreous appears to become almost imperceptibly more viscous. This has been observed within six hours of a single dose to the eye of 100 s/r.

After this initial stage of greater viscosity the prolapsed vitreous begins to retract into the globe, and in about forty-eight hours the process of retraction is very nearly completed. What is of value and interest is that the vitreous remains clear without any perceptible abnormality, giving maximum vision; the period of observation is five years.

Effect on ocular signs and symptoms.—Symptoms characteristic of ocular irritation—lacrimation, photophobia and pain—need further mention. X-rays relieve pain as in herpes ophthalmicus where it is of nerve origin; pain produced by mechanical causes, such as we find in glaucoma, is not helped to any appreciable extent.

Intra-ocular tension.—The summation effect of X-rays is apt to raise intra-ocular tension for no discernible reason. It is well to use the intra-ocular tension as a "control" whenever diathermy is applied.

Injection of uveal tract.—X-radiation quietens the irritable eye. Purple injection of the uveal tract fades away gradually and the eye regains its normal appearance.

out only by an experienced radiologist, as an excess dose might fail to produce the desired effect, or might even delay healing.

Summary of the results.—In a small series of cases the results were uniformly successful. They were better when we had the cases early, for then we could be sure of preventing loss of bone by sequestrum formation. In at least three cases an apparently inevitable amputation was avoided. The sinuses healed, the evidence of inflammation of the soft parts disappeared, and the patients lost all fear of using the affected digit.

At the same time, and in a matter of weeks, the appearances of the radiographs quite changed. The ghost-like bone recalcified, and its pattern reappeared. Destruction of the joint surfaces and loss of bone substance were the two factors that gave rise to permanent radiographic changes.

The conclusion from clinical observation is that X-rays did something that neither local nor general antibacterial therapy was able to accomplish.

Dr. Francis Freund: *Action of X-rays on inflammation.*—The main reason for the healthy scepticism about this treatment is that the mode of action is unknown. Any explanation should correlate the histology of the normal course of inflammation with the histology of the changes caused by X-rays. The whole conception about inflammatory reaction has changed fundamentally in the last twenty years.

In recent editions of textbooks on pathology it is stated, that in acute and chronic inflammations local cellular reaction plays the major part, and emigration of cells from the vessels a minor part. The cells of the vessel walls, the adventitia cells, the cells of the reticulo-endothelium and even of the alveolar epithelium of the lungs, in short all cells of mesenchymal origin, can change into inflammatory cells. When healing takes place the mononuclear inflammatory cells change back again into fibrocytes and fibrous tissue. The polymorphonuclear inflammatory cells disintegrate and are not capable of differentiation. Cells of mesenchymal origin regain the faculty of differentiation in post-embryonic life under the following conditions: (1) Myelosis, (2) Inflammations, (3) Callus formation.

It is an obvious conclusion that X-rays might influence this differentiation. Before going into the study of the action on cells, the action on bacteria should be discussed.

No action on bacteria has been described when a small dose of X-rays is applied. Dr. Cadness-Graves and I have recently experimented on bacteria of all sorts and under varied conditions, and we could not find any definite evidence of a loss of vitality of the bacteria. One would expect that an increase and not decrease of the dose would be more beneficial if bacteria were affected and, in addition, aseptic inflammations respond equally well to the treatment. It is therefore justifiable to state that the action of X-rays on inflammations is not bactericidal.

I inflicted small wounds in the centre of the cornea of animals under local anæsthesia. Rapid healing occurred compared with controls. As there are no vessels in the centre of the cornea the healing effect cannot therefore be attributed to an action on blood-vessels, as some authors assume. Having eliminated the possibility of any effect on bacteria and vessels, we can turn now to the action on tissue cells.

Action on polymorphonuclear leucocytes.—It is widely believed that destruction of polymorphonuclear leucocytes is responsible for the healing effects. That these provided by a simple application of the principles of the effect of X-rays on inflammatory processes. Experimental work carried out by Freund in 1929 (*Strahlentherapie*, **33**, 375) and by Fukase, 1929 (*Virchow's Arch.*, **273**, 794) has shown that X-rays had a beneficial effect on the recovery from inflammatory lesions. These observers investigated the behaviour of mesenchymatous tissues under the influence of X-rays, and their conclusions were that the differentiation of inflammatory cells into fibroblasts and fibrocytes was stimulated. In bone lesions they demonstrated that re-ossification was promoted in conditions characterized by deficient bone formation. Dr. Finzi and Dr. Phillips started X-ray treatment of osteomyelitis of the fingers at St. Bartholomew's Hospital in 1939. The radiographs of a case treated by them (*Brit. med. J.*, 1943 (i), 34) show extensive destruction of bone and complete regeneration in a case in which the question of amputation had been seriously considered. The dose used was 30 to 80 r, and 160 kV. filtered with 0·5 mm. of copper.

We wished to use this treatment for patients of the Emergency Hospital at Oster House, St. Albans, but we were unwilling to send the patients to London during the worst period of the flying and rocket-bomb attacks, and Dr. Freund suggested that we should use the diagnostic X-ray plant of the hospital. The radiographs [*shown*] demonstrate the results obtained by this simple method (*see* figs. 1 and 2).

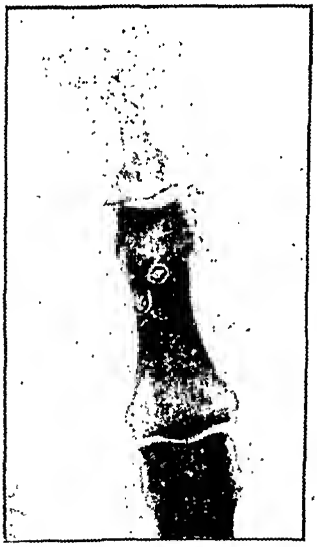


FIG. 1.—N. H. Osteomyelitis of four weeks' duration. Organism: *Staphylococcus fluorescens*. Daily irrigation with penicillin without success.

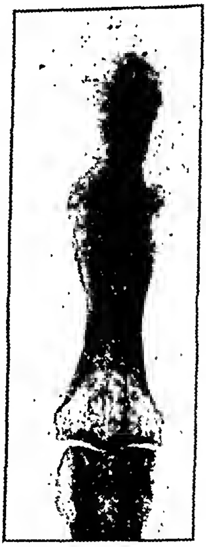


FIG. 2.—After screening with the diagnostic tube in the normal screening distance, 60kV./3ma. three minutes weekly, for five weeks.

The septic digits were screened, using the screening voltage of routine fluoroscopy at the usual screening distance. The dose required was calculated as one-tenth of the erythema dose. Twenty minutes' exposure with the diagnostic apparatus under ordinary screen conditions was taken as being an erythema dose, and two to three minutes as a suitable dose for our purpose. This dose (50 to 75 r) was given once a week for three to five weeks. Being only one-tenth of the erythema dose it could not inflict burns. Nevertheless, Dr. Freund insists that the treatment should be carried common occurrence of delayed repair. *Small doses of X-rays initiate repair or prevent exuberant local reaction by their differentiating effect upon inflammatory cells.* Under the assumption that bacteria or leucocytes should be destroyed, too high and too many doses are given. Differentiation takes time and requires not more than 50 r, once a week. The treatment of osteomyelitis and of inflammatory conditions of the eye are only easily demonstrable examples of the general principle involved. The clear conception of what we are doing makes the enumeration of indications superfluous and leaves it to reason. Even less apparent inflammations are excellent indications for X-ray therapy. If, for instance, skin grafts are not readily taken, a small dose of X-rays checks the unwanted local reaction, and almost invisible scars can be achieved.

Here again we have only another example of the power of X-rays to exercise control, rather than to destroy.

REFERENCES

DESJARDINS, A. V. (1942) *Radiology*, 38, 274.
FINZI, N. S., and FREUND, F. (1943) *Brit. med. J.* (i), 34.
FREUND, F. (1928) *Virch. Arch.*, 269, 501.
—— (1930) *Virch. Arch.*, 279, 30.
FUKASE, S. (1929) *Virch. Arch.*, 273, 794: and 277, 69.
HEIDENHAIN, LOTHAR, and FRIED, C. (1924) *Arch. klin. Chir.*, 133, 624-655.
——, ——, —— (1924) *Klin. Wschr.*, 3, 1121.
PENDERGRASS, E. P., and HODES, P. J. (1941) *Amer. J. Roentgenol.*, 45, 74.
WARTHIN, A. S. (1905) *Int. Clin.*, ser. 15, 4, 243.

Dr. N. S. Finzi: During most of my earlier radiological career, I was trying for many years to persuade radiologists to give sufficient dosage in malignant disease in order to attempt to cure, and not merely to palliate. Having eventually succeeded in this, I am now having equal difficulty in trying to persuade them to give small enough doses in inflammatory conditions. I first realized this at the International Congress in Stockholm in 1928, when a report was presented showing better results in tuberculosis with smaller than with larger doses. Since then my results, both in tuberculosis and other inflammatory conditions, have very definitely improved as the result of the use of smaller dosage. I admit that successful results can very often be obtained with medium dosage, but they are not so good or so frequent as with small dosage, and the length of time over which the treatment can be spread is very much less. On the whole, the dosage to be aimed at is 50 to 60 r lesion dose, with penetrating rays, as a start, gradually decreasing to about 40 r once every five to seven days. With less penetration, smaller doses must be given. As an instance, when Mr. Ralph Phillips first started treating osteomyelitis of the finger with X-rays, he used 100 r twice a week. When I persuaded him to use 50 r every five to seven days, the results were not only as good, but better.

One extraordinary feature which one observes in these osteomyelitis cases is the disappearance of sequestra. What any radio-diagnostician would be quite certain is a sequestrum will very often become incorporated in the new bone, with no evidence, either radiologically or clinically, of the persistence of a sequestrum.

I want, in particular, to draw attention to the treatment of arthritis with these smaller doses. One must, of course, remember that there is always much more absorption of the rays by bone than is given in any dosage curves. It amounts to 15 or 16% extra when using 200 kV. and a Thoraeus filter, and is correspondingly greater when using rays of less penetration. I find that, when this is taken into consideration, and the dose regulated accordingly, the results obtained in some of these cases are very striking. But I also use an adjuvant, which is not known to cells are destroyed is based on investigations which Warthin carried out in 1905. He tried to prove that the disappearance of leucocytes in the blood-stream of leukæmic patients is due to destruction of leucocytes by the direct action of the rays. This very plausible explanation is *not* borne out by facts. In exudates which I produced experimentally in the dorsal lymph-pouch of frogs, an increased disintegration of polymorphonuclear leucocytes can be observed after irradiation. I never attached much significance to these changes, because disintegration of polymorphs takes place in any exudate and only speeding up of a breakdown into pus might be explained.

I had the rare opportunity to treat a patient with myeloid leukæmia who had numerous myeloid nodules in the skin. In a biopsy made before and after treatment the differentiation of cells of mesenchymal origin into mononuclear leucocytes can be clearly shown. After irradiation the change into fibrocytes and fibrous tissue can be seen. There is no evidence of young fibroblasts, but the actual cells have changed, the nucleus has become dense and stretched and layers of fibrous tissue surround the nucleus like onion skins.

We know that spontaneous healing of such myeloid nodules does not occur. The cure has been achieved by the differentiating action of the X-rays. It is a reasonable step to assume that under inflammatory conditions mononuclear leucocytes might likewise change into fibrocytes and fibrous tissues.

Action upon mononuclear leucocytes.—I studied the normal course of inflammation in the frog's tongue, an experiment recommended by Cohnheim.

The slides showed widespread cellular activity going on outside the vessels, before any emigration from the vessels had occurred. The fragmentation of the nucleus and the formation of polymorphs in the early stage of inflammation could be demonstrated.

After these findings I thought that the local growth of inflammatory cells might be prevented by prophylactic X-ray treatment and rapid repair achieved. Wounds inflicted on the skin of rabbits healed quicker in the irradiated part. The histological slides confirm the macroscopic appearances. There is an exudate in the part not irradiated, there is no inflammatory reaction in the irradiated one.

In order to exclude infection and to have an object that can be easily demonstrated, the traumatic inflammation after fracture was studied before and after irradiation. The fibula of rabbits was fractured on both sides. On the irradiated side the callus formation was less, but firm bony union occurred earlier. The histological slides show, after five days, mononuclear granulation tissue, but fibrocytes on the irradiated side. After eight days you see cartilage cells appear, if not irradiated, and fibrocytes and fibrous tissue, if irradiated. The dose was 400 r; if the dose is increased to 1,600 r, delayed union takes place. The fibrocytes assume the character of embryonic mesenchymal cells and after three weeks the differentiation into numerous capillaries takes place, preventing bony union for several weeks. Even a dose of 400 r shows changes of the fibrous tissues, specific of X-ray irradiation. It serves as a warning to give very small doses in order to avoid damage to defence and repair.

DISCUSSION AND CONCLUSION

The rationale of the osteomyelitis treatment, discussed by Miss Baker, can be explained by the experiments shown. Debris, devitalized tissues, constitutional and nutritional causes often delay repair, long after the danger of general infection has passed. We can visualize delayed bony union, but this is only part of the

Clinical Section

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[*November* 8, 1946]

Myelosclerosis with Leukæmoid Blood Picture.—E. IDRIS JONES, M.D.

Male, aged 51. Plumber for thirty years, store-keeper for last eight years. Admitted to hospital September 1942 because of increasing pallor and loss of energy for previous six months. No other symptoms.

On examination.—Pallor, spleen enlarged 2½ in. below costal margin and liver 2 in. down. Slight enlargement of inguinal glands, rest normal. B.P. 122/70. Heart, lungs, C.N.S.—N.A.D.

Blood-count (18.11.42).—R.B.C. 3,140,000; Hb. 54%; W.B.C. 8,700 per c.mm. 5% reticulocytes. Polys. 68%, eosinos 1%, lymphos. 22%, monos. 2%, premyelocytes 4%, myelocytes 3%. 15 normoblasts per 100 white cells.

Radiography of bones showed dense sclerosis, especially at base of skull. Sternal marrow not obtained by puncture so sternum was trephined and sections made of bone. These showed increased trabeculation with increase in collagen fibres and scanty islands of bone-marrow with little or no fat.

Anæmia did not respond to treatment, splenomegaly increased but blood picture remained approximately as above until June 1946. Increase in immature white cells then occurred and patient has developed dyspnœa and œdema of legs. Spleen now well below umbilicus with systolic murmur audible over it.

Blood-counts:

3.6.46: R.B.C. 2,600,000; Hb. 50%; W.B.C. 33,200. Immature red and white cells present.

9.9.46: R.B.C. 3,140,000; Hb. 50%; W.B.C. 54,700. 30% immature white cells and 14 immature red cells per 100 white cells.

4.11.46: R.B.C. 2,750,000; Hb. 40%; W.B.C. 82,000. Polys. 45%, basos. 6%, monos. 3%, premonocytes 4%, lymphos. 3·5%, metamyelocytes 12%, myelocytes every radiologist. This is the application, in the case of the upper limb, of X-rays to the lower cervical and upper dorsal region; and, in the case of the lower limb, to the lumbosacral region, aiming again at a similar lesion dose. I discovered this by accident when treating a patient with X-rays for a stiff neck. She had had for many years very bad arthritis of the hands. As a result of treating the neck, the hands improved so much without any direct treatment that they were better than they had been for twenty years. I discovered later on that the treatment was not new, as it had been used in America three years before, but I have unfortunately forgotten the name of the investigator who published the work.

We got excellent results at St. Bartholomew's Hospital in cases of spondylitis ankylopoietica by using a dose of 75 r at 60 or 70 cm. F.S.D. on the surface, which meant a dose of 50 r at the lesion, and repeating this every five days. There may be cases which require higher dosage, but most of them will respond to this smaller dosage.

While on the subject of arthritis, I must mention the results in sciatica and other forms of neuritis, including the post-herpetic variety and also the results in fibrositis. In sciatica there is often a tender spot at a certain point in the buttock, and if this exists, the case can nearly always be cured.

Another condition where I have treated a number of cases with smaller doses is mastitis, my most striking case being one in which the lumps were so large that both the surgeon and I felt that one breast must be removed to make sure that our diagnosis was correct. When this had been done, I treated the other breast and the lumps completely disappeared and she remained cured for many years.

In view of the low dosage employed, the treatment can be continued over very long periods if necessary, without any danger of permanent damage to the skin or subcutaneous tissues.

Conclusion.—A case of primary xanthomatosis with biliary cirrhosis.

Dr. F. Parkes Weber agreed that the case was a perfect example of tuberous (elbows and knees) and plane (hand creases) xanthomata of Thannhauser and Magendantz's hypercholesterolæmic group of primary essential xanthomatosis (as described by them in 1938) with jaundice due to xanthomatous biliary cirrhosis. In a booklet on "Cutaneous Xanthoma and Xanthomatosis of Other Parts of the Body" (1924, p. 10) Dr. Weber referred to a number of cases of xanthomatous biliary cirrhosis, but failed to recognize that they formed an important part of the group afterwards (1938) distinguished by Thannhauser and Magendantz as their hypercholesterolæmic group.

Sarcoma of Bronchus.—IVOR LEWIS, M.S.

C. C. H., aged 14, was admitted to the North Middlesex Hospital on June 23, 1946, complaining of shortness of breath for three months, with some pain in the right chest, some cough, a little phlegm but no hæmoptysis. The day before admission he became much more breathless; previous history of occasional bronchitis, nothing suggestive of aspiring a foreign body.

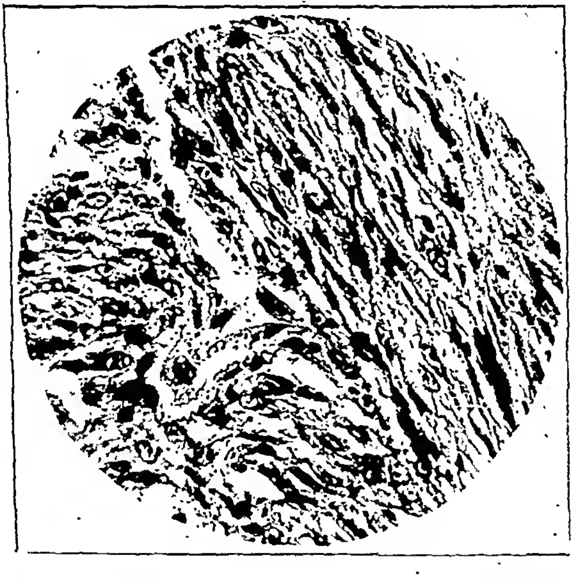


FIG. 1.—Biopsy, October 10, 1946. The section shows well-defined fibroblasts cut in several planes. In this instance the cells on the average are more protoplasmic than in the second biopsy. Masson's trichrome stain. × 400.

On examination.—A pale, very tall boy (5 ft. 10 in.), moderately breathless and a little blue; T.101, P.120. There is no clubbing, trachea and heart greatly displaced to the right, dull, right base. A little sterile, straw-coloured fluid was obtained from the pleura. X-ray at this time (June 25) showed widening of the mediastinum with much displacement of heart to the right. His pyrexia disappeared.

July 9: X-ray—the right upper lung now entirely opaque except for a small area of the R. upper lobe, with the heart completely to the right of midline.

21·5%, premyelocytes 2%, myeloblasts 3%. 7 normoblasts, 4 erythroblasts and 1 megaloblast per 100 white cells.

Blood uric acid 2·9 mg.%.

Total plasma protein 6·8 grammes%. Albumin 3·3 grammes. Globulin 3·2 grammes. Fibrinogen 0·3 gramme.

Dr. F. Parkes Weber remarked that in such cases the question arose: (1) Is the leukæmoid blood picture secondary to the myelosclerosis, or (2) does the myelosclerosis represent a bone-reaction which may be explained teleologically as an attempt to oppose a leukæmic expansion of the bone-marrow? In the present case it seems more probable that the leukæmoid blood picture represents a regenerative reaction towards the damage done by the myelosclerosis to the hæmopoietic organ (the bone-marrow).

Dr. Weber thought that X-ray examination in the present case shows that the myelosclerosis is only part of a general osteosclerotic change of the nature of osteopetrosis, that is to say, "marble bones." The case is not unlike Albers-Schönberg's original case (1904) of "marble bones", though the bone changes are less. The patient in that case was not a child, as in many cases of "marble bones", but was an adult man, who died in 1927 in his 49th year, and whose case was afterwards fully described by F. Reiche, 1929 (*Münch. med. Wschr.*, 76, 1078).

Xanthomatosis.—C. P. PETCH, M.B., M.R.C.P. (for Professor de WESSELOW, D.M., F.R.C.P.).

A woman of 55 complained that for thirteen months she had suffered from discoloured areas of the medial portions of the upper and lower eyelids on both sides. These were treated a year ago by cauterization and it was noted at that time that she was slightly jaundiced and had a large liver. Since then the discoloured areas have increased in size and similar patches have appeared on both elbows and both knees. The palmar creases are also the site of the yellow deposits.

The jaundice has increased slowly. She has had no other symptoms and her previous health has been consistently good, apart from hysterectomy for fibroids in 1937.

On examination.—Marked jaundice with heavy xanthomatous deposits in the areas previously described and on the great toes. The liver is enlarged about 5 in. below the costal margin and is hard and smooth. The spleen is palpable. There is no abnormality in the C.V.S. Blood-pressure 145/85. The urine is normal.

Investigations.—X-rays of chest, skull and lumbar vertebræ show no abnormality, apart from small areas of patchy sclerosis in the cranial vault. No calculi in gall-bladder region. E.C.G. shows no significant abnormality.

Blood: Hb. 84%; W.B.C. 5,600. Polys. 69%, lymphs. 26%, eosinos. 1%, basos. 1%, pathological lymphos. 2%. Van den Bergh reaction direct positive. Fasting blood sugar 95 mg.%. Normal glucose tolerance curve.

Plasma proteins 8·88%—albumin 3·75%; globulin 5·31%.

Plasma lipids—mgm. per 100 c.c.

Non-phospholipid fatty acids	452	Free cholesterol	311
Neutral fats	226	Estercholesterol	328
Phospholipids	743	Total cholesterol	639

Liver function by the hippuric acid test was 110% of normal.

Prothrombin time 19 seconds.

Urinary urobilinogen 1·8 mg. per 100 c.c.

Fæcal urobilinogen 120 mg. per 100 c.c.

in Von Reckinghausen's disease. Sections prepared from several parts of the tumours of the stomach showed that these possessed a different and unusual structure. These tumours were composed of epithelial cells, small in size, oval or spheroidal in shape. The nuclei were round or oval, and the cytoplasm scanty and sometimes vacuolated. Special stains for fat, mucin, and glycogen gave negative results. An occasional small mononucleated giant-cell was seen. Rosettes were not found. The cells were separated by an abundant intercellular substance, which by special staining was seen to contain a reticulum, in which the cells were disposed in fascicular fashion. It is thought that the tumours are neuro-epitheliomatous in structure and are composed of neuro-ectodermal cells displaced during development with the peripheral nerves (fig. 2).

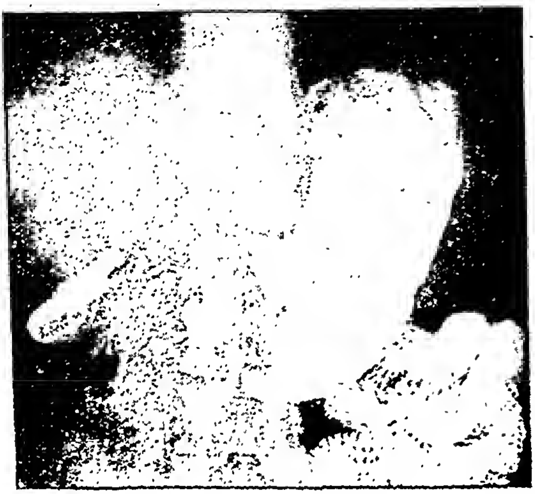


FIG. 1.

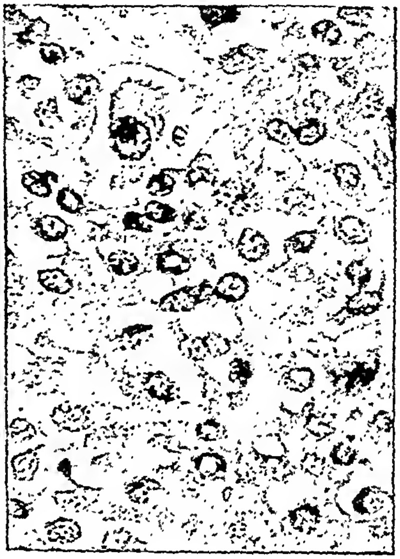


FIG. 2.

FIG. 1.—Stomach, prone, showing circular filling defects in antrum.

FIG. 2.—Photomicrograph of representative part of tumour of stomach showing the characteristic cells. ×430.

Cirsoid Aneurysm.—K. W. PRIDDIS, F.R.C.S. (for Mr. ALAN SMALL).

E. P., female, aged 17½. Clerk.

History.—January 1945: She presented at Tilbury Hospital complaining of inequality in the size of her legs. Apart from this she experienced no subjective symptoms nor incapacity.

June 1945: She fell downstairs and bruised her right knee. She was admitted to London Hospital where after a week in bed an ulcer developed 1 in. below the right patella. It has been present ever since. While still in hospital at rest she suffered three secondary hæmorrhages, the last one being massive. It was controlled by digital compression of the femoral artery and later by a firm pressure

July 18.—Bronchoscopy (I. L.) showed the orifice of the R. bronchus to be filled by a soft, yellowish white growth, a little firmer than brain tissue. Only a small chink remained open. The attachment of the growth extended right up to the carina. It was not lobulated. Large pieces of it were removed by forceps, securing good entry into the bronchus; a fair amount of bleeding.

X-ray next day already showed re-aeration of about half the R. lung.

August 7 to 29: Course of radiotherapy, Total 6,353 r.

August 10: Re-bronchoscoped. There was now a smooth prominence, rather like an inflamed turbinate viewed from the posterior nares.

September 3: X-ray showed normal position of heart with practically complete aeration of the R. lung.

October 10: Bronchoscopy; only a small residual growth, 1 cm. long × 2 mm. × 2 mm. arising from the posterior wall of the bronchus at its junction with the trachea.

Biopsy.—July 18, 1946 (Mr. T. H. C. Benians): "Growth is made up of spindle cells widely separated by œdema and arranged in whorls. Considerable variation of the nuclei. I think the tumour should be considered a fibrosarcoma."

October 10, 1946 (Dr. J. F. Heggie): "Still shows a cellular growth composed of spindle cells arranged in irregular bundles. They appear more protoplasmic and more actively growing than previously. Despite the relative absence of mitotic figures the condition is sarcomatous."

Neurofibroma of Stomach in Von Recklinghausen's Disease.—T. W. MIMPRISS, M.S.

Male, aged 68.

Family history.—Grandfather, father and daughter have neurofibromatosis. Patient shows cutaneous manifestations of this condition very well, otherwise has been fit.

Previous history.—Indigestion and epigastric pain for eighteen months, with flatulence and vomiting. Has lost 1½ st. in weight.

On examination.—Large abdominal tumour, 4 in. in diameter, moving on respiration, palpable at level of umbilicus.

Barium meal showed filling defect of stomach suggesting large polypus (fig. 1).

In view of his general condition tumour was diagnosed as neurofibroma.

Test meal showed no free HCl, lactic acid present.

At operation the tumour was found to be growing from the greater curvature of the stomach. The large part was subperitoneal and there was a smaller submucous portion obstructing the lumen of the stomach. There was one smaller submucous tumour present in the stomach. Billroth I partial gastrectomy performed.

Patient has made satisfactory progress since then.

Histological report (Dr. J. Bamforth).—Histological examination of one of the cutaneous lesions showed the typical appearances of a neurofibroma as usually seen

Section of Surgery

President—Ernest Finch, M.D., M.S., F.R.C.S.

[*November 6, 1946*]

DISCUSSION ON THE TREATMENT OF ACUTE PERITONITIS

Mr. John Morley: I propose to discuss in the broadest terms the treatment of acute peritonitis secondary to infection from the hollow viscera, whether that infection is due to military or civil trauma, to the activities of the surgeon, or to the spontaneous processes of disease.

I am old enough to remember the period of flushing and purging in acute peritonitis. Irrigating fluid under considerable pressure was poured into the peritoneal cavity with the object of flushing out all infective material. The more enlightened used normal saline in this misguided effort, others used various antiseptic fluids of varying degrees of toxicity, but the result was almost uniformly disastrous. If the patient did not succumb to shock, which was usually profound, the invading organisms were spread through the peritoneum, and the reflex inhibition of intestinal movement was made more complete. Then, warming to his work, the surgeon would attempt to overcome the intestinal paralysis by heroic doses of purgatives, repeated hourly "until something happened". What usually happened was the death of the patient, preceded in some cases by a futile enterostomy. About this period there was a great belief in the efficacy of drainage, and the patient with peritonitis would be left bristling with tubes in various quarters of his abdomen, though Nature soon sealed them off, if she was granted time, and they drained little but their own track.

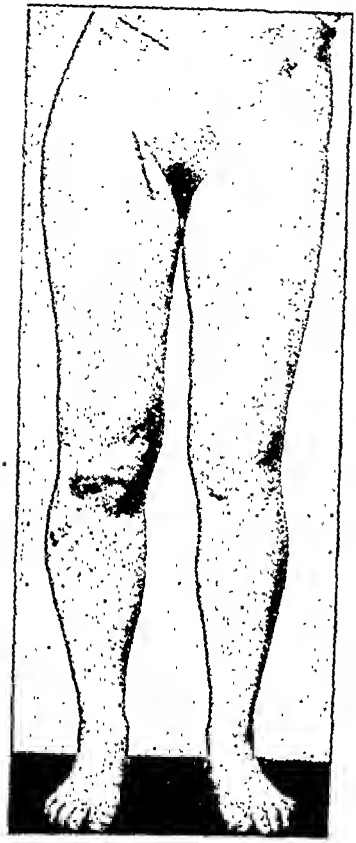
It was a great step forward when this vigorous and ill-advised flushing was abandoned, and gentle sponging of the peritoneal cavity with swabs rung out of warm normal saline took its place, later to be replaced by suction. Spinal anæsthesia, by means of which the surgeon gained the most complete relaxation and ease of access, came into more general use.

But the greatest advance in treatment about this time was the realization of the important part played in peritonitis by loss of water and sodium chloride from the blood; and the practice of replacing them by normal saline given at first *per rectum* or subcutaneously, and later by the intravenous route.

A further step forward came with the introduction of the Ryle's tube. Designed for gastric analysis, it was soon applied to gastric and duodenal suction in peritonitis and intestinal obstruction, with great relief from distension and vomiting.

Sir Henry Dale's discovery of the fundamental part played by acetylcholine in the augmentor mechanism of the gut brought about a certain tendency to revert to the fashion of purging in peritonitis, though now the purging was done with a hypodermic syringe. For a time acetylcholine, eserine, or pitressin were largely used in the hope of overcoming the intestinal inertia of peritonitis, but the results were on the whole disappointing, and we soon came back to the practice of relying chiefly on intravenous fluid, gastric or intestinal suction, and avoidance of fluids by the mouth, giving the antibacterial defences of the body a chance to do their beneficent work unhampered. (In milder cases those drugs that stimulate peristalsis undoubtedly have their use.) And then came the crowning mercy of chemotherapy, first with the sulphonamides and later with penicillin.

Principles of treatment.—Since the vast majority of the cases of peritonitis we are called upon to deal with are secondary to perforations of the alimentary tract, I would put first the closure of the perforation. This means most commonly in civil practice, the removal of a perforated appendix or suture of a perforated duodenal ulcer. If the patient is already showing signs of dehydration, intravenous bandage. *During her stay she was treated ineffectively by deep X-ray and later radon ointment.*



NOTE: (1) The increase in length of the right limb illustrated by the difference in height of anterior superior iliac spines marked with crosses. (2) Increase in girth. (3) Chronic ulcer in the centre of the lower and larger hæmangioma, with two large tortuous arteries medial to the ulcer.

On direct questioning.—She has 5 hæmangiomata around her right patella, which have enlarged proportionally with her general growth.

On examination.—Right Leg: Within 2 in. of the patella lie five dull bluish cutaneous hæmangiomata. In the centre of the largest one (2½ in. × 2½ in.) below the patella, is a typical chronic ulcer (1 in. × ¾ in.).

The whole region of the knee is enlarged, soft, boggy and gently pulsatile. Two large tortuous arteries are visibly and palpably pulsatile on the medial aspect of the ulcer and passing beneath it. A loud high-pitched systolic murmur is present, maximal over the ulcer and on the lateral side of the knee-joint and propagated above the mid-thigh and below as far as the ankle.

Measurements of Limbs.—

Length: Left leg 33 in., right leg 34 in., the increase being equally shared by tibia and femur.

Increase in girth: Thigh 1 in., lower leg ¾ in., knee-joint 1¼ in.

Straight X-ray.—Right femoral condyle ⅛ in. wider than left. No bony rarefaction.

Arteriogram.—14 c.c. Diodone were injected with the femoral artery controlled proximally to site of injection. The concentration of the dye in the tortuous vessels was too poor to reproduce adequately in photographic form. The extent of the lesion was from 3 in. above to about 3 in. below the patella. Three of the large vessels of the aneurysm were of the order of size of the radial artery.

Cardiovascular system.—Heart: Auscultation—no accompanying murmurs. Size—normal clinically, and by X-ray and screening.

Blood: R.B.C. 5,000,000 / c.mm. Hb. 95%.

Blood-pressure and pulse-rate.—At rest, B.P. 135/60; P.R. 82/min. Right femoral artery occluded, B.P. 150/100; P.R. 80/min. Left femoral artery occluded, B.P. 140/65; P.R. 80/min.

Mr. A. Dickson Wright: These arterial types of arteriovenous aneurysms of the legs are very serious cases, liable to terminate fatally from massive hæmorrhage from the associated ulcer during sleep. They frequently end with amputation and often it is hard to get above the pathological condition so that trouble develops in the stump. For this case I would recommend exposure of the femoral artery from groin to the popliteal space with ligature of every branch of the exposed artery. The circulation to the foot is thus assured while the cirsoid vessels are deprived of their arterial connexion.

Chemotherapy.—While everyone will agree that chemotherapy gives us an additional weapon of great value, there is still no approach to unanimity as to which is the best drug to use, or as to the best manner of its application. Intraperitoneal sulphonamides have been widely used with some very promising results. It will be generally agreed that it is a bad practice to dump masses of sulphonamide powder into the peritoneum. It becomes walled off in clumps by adhesions, and these may be a real danger later. A sounder method is to introduce the powder stirred up in normal saline. But what drug? Vaughan Hudson and Smith recommend 15 to 20 grammes of sulphanilamide suspended in 60 to 70 c.c. of normal saline, and with this drug they reduced their mortality in grave general peritonitis and resection of gangrenous gut from 55% to 8·3%. Gardiner rather favours sulphapyridine, also suspended in saline, as it showed the slowest absorption rate and lowest toxicity of any drug he employed.

Young and Warren Cole use phthalyl sulphathiazole or succinyl sulphathiazole intraperitoneally on the grounds that they produce no adhesions and are lethal to coliform organisms.

Fauley *et al.* produced experimental gangrenous appendicitis in dogs by ligating the blood-vessels of the appendix, and obtained strikingly successful results when treatment by intramuscular penicillin was started one hour after the operation.

George Crile, Junior, has recently described a series of 50 cases of peritonitis, either general or local, secondary to appendicitis, treated by 100,000 units of penicillin every two hours for several days, with remarkably good results. There was only one death, from mesenteric thrombosis, and in all the others the infection was controlled by penicillin.

The prophylactic treatment of post-operative peritonitis.—In conditions involving partial obstruction, such as carcinoma of the colon, the fear of intraperitoneal leakage and fatal peritonitis has in the past dictated the custom of operating in multiple stages, starting with a colostomy for the relief of obstruction. Where obstruction is not too complete, most surgeons are finding that succinyl sulphathiazole or phthalyl sulphathiazole given by mouth in adequate doses for three or four days before operation causes such a reduction in the bacterial flora of the gut that primary resection and suture can be carried out with impunity in many cases where it would have been fatal before the use of these drugs. They may well be supplemented by intraperitoneal sulphonamides, but the relative sterilization of the bowel contents is the main objective.

Within recent months, we have witnessed two vigorous tugs at the pillars of the house of surgical orthodoxy. I refer, of course, to Spalding's attack on the time-honoured Fowler position, and Hermon Taylor's advocacy of the non-operative treatment of perforated peptic ulcer. In my view the theory that the Fowler position is the best position to protect the patient from subphrenic abscess formation and from post-operative chest complications does not emerge unscathed from Spalding's attack. Without subscribing to all his arguments about the hydraulics of the subphrenic spaces, I am impressed by his contention that the pneumoperitoneum that follows laparotomy is a source of pain and limitation of breathing in the Fowler position, for I know that pneumoperitoneum induced for radiography of the solid viscera produces marked shoulder-tip pain if the patient sits up, but little or no pain while he is recumbent. I do not follow him in his argument that the Fowler position is uncomfortable to the patient. To my mind, it is too comfortable, and as the nurse is apt to think that his chest is safe in that position, the patient is allowed to lie still for hours with the base of his lungs immobile, and the veins of his calves stagnant, when what he needs for both lungs and limbs is very frequent movement and change of position.

By Hermon Taylor's plea for the expectant treatment of perforated peptic ulcer as a routine I find myself much less convinced. One may concede that in a saline or plasma, with gastric suction by a Ryle's tube, should be started an hour or two before the operation.

The operation itself, necessary though it is, inevitably adds somewhat to the risk of paralytic ileus. If we examine any case of diffuse peritoneal irritation, such as a perforated duodenal ulcer with widespread escape of duodenal contents into the peritoneum, we find from the first a silent abdomen on auscultation. This silence is not due to paralysis of the gut at first, but to active inhibition of all movements by the splanchnic inhibitory reflex. The afferent nerves of this reflex are the sensory fibres supplying the parietal peritoneum, and the efferent nerves are the sympathetic inhibitory fibres to the gut. It is in essence a beneficent protective mechanism, evolved to prevent diffusion of septic material in the peritoneum by the ceaseless movements of the small intestines. Only later, when the gut is distended with gas and fluid, and œdematous from inflammatory changes and failing circulation, does its wall become truly paralysed, and there comes a stage when the paralysis is irreversible by any treatment and the only end is death. The term paralytic ileus emphasizes this terminal stage. I prefer the term *inhibitory* ileus which emphasizes the initial stage, when treatment can do some good.

Now Nature, in evolving the splanchnic inhibitory reflex, took no account of surgical intervention. Every time we open the abdomen and traumatize the sensory nerve-endings in the parietal peritoneum we bring this reflex into action—hence the post-operative "wind" pains after any abdominal operation. Where peritoneal irritation has already produced an inhibitory ileus, our incision adds to the stimulus and increases the tendency to ileus. The best way to avoid this (though only in part) is to operate under spinal anæsthesia, which blocks the inhibitory reflex for the duration of the anæsthesia. In proof of this, one may see intestines bathed in pus contracting in active peristalsis, when exposed under a spinal anæsthetic, though this does not occur in the later stage of true intestinal paralysis.

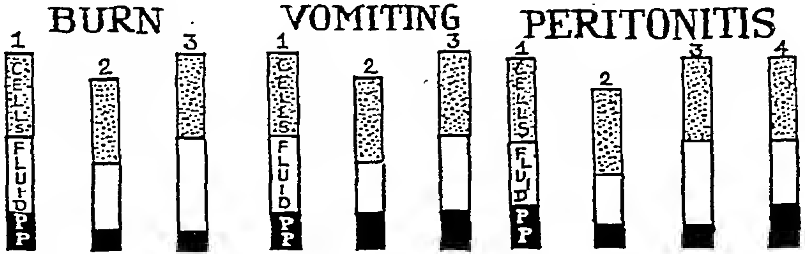
There is a fundamental difference between this inhibitory or paralytic ileus (sometimes, but not very happily, called adynamic ileus), and mechanical ileus. Peritonitis often leads to mechanical ileus by causing fibrinous or fibrous adhesions that result in kinking, torsion or compression of the bowel. Here we do not find at first the silent immobile abdomen, but noisy exaggerated peristalsis and the colicky intermittent central pains of obstruction. Only in the terminal and hopeless stage of mechanical ileus do we find the silent abdomen.

It is in mechanical ileus due to recent adhesions that the Miller-Abbott tube has proved invaluable, provided that one is reasonably sure there is no strangulation of the gut. It is also of great value in inhibitory ileus if one can get it through the pylorus, but this is often very difficult. Happily, however, a Ryle's tube in the stomach with continuous suction, though somewhat less effective than the Miller-Abbott tube, works very well. The use of the Miller-Abbott tube has practically superseded enterostomy.

To return to the operation: It is carried out with the least possible trauma. This means, in addition to spinal anæsthesia, an adequate incision, and suction rather than sponging to cleanse the peritoneum of infected fluid.

Should the peritoneum be drained? In perforated peptic ulcer, I have not drained a case (apart from subphrenic abscess) for the last twenty years, and I am sure drainage is unnecessary and likely to give rise to the most dangerous form of adhesions. In peritonitis from a gangrenous appendix, I do not drain the peritoneum unless an abscess cavity is very prone to bleed, and then only for twenty-four or forty-eight hours, but I always drain the contaminated abdominal wall. In general, I believe that drainage of the peritoneum does very little good, and that the peritoneum can be trusted to destroy any organisms that are left when the perforation has been closed and gross fluid sucked out. But when in doubt, there is no great harm in draining for a day or two.

In addition in acute peritonitis as in any other infective process, the albumin globulin ratio of the plasma proteins changes; the albumin level falling and the globulin level rising. The importance of this is that the plasma globulins exert an osmotic pressure which is only about one-third of that exerted by an equivalent quantity of plasma albumin.



	BURN 1	BURN 2	BURN 3	VOMITING 1	VOMITING 2	VOMITING 3	PERITONITIS 1	PERITONITIS 2	PERITONITIS 3	PERITONITIS 4
R.B.C.	4·5	6·0	4·5	4·5	6·0	4·5	4·5	6·0	4·5	4·5
Plasma protein	7·5	7·5	5·0	7·5	10·0	7·5	7·5	7·5	5·0	7·5

The accompanying diagram illustrates the effect of acute general peritonitis on the blood volume, the packed cell volume or hæmatocrit reading, and the protein content of the blood. It compares these with the changes which occur in burns and severe vomiting. The height of each column represents the total blood volume, the spotted area the red and white blood corpuscular volume, the clear area the water, salt content, &c., and the black area the plasma proteins. Column 1 under each heading is the normal. Column 2 indicates the position after fluid and protein loss have reduced the blood volume. Column 3 shows what happens after the blood volume has been restored by glucose saline infusion; column 4 demonstrates the theoretical state of affairs after giving both plasma transfusions and glucose saline infusions to a patient with acute general peritonitis. The figures below indicate the red blood corpuscular count and the plasma protein level.

It will be seen that the changes in acute peritonitis are a combination of those found in burns and severe vomiting. The initial hæmoconcentration results in a raised packed cell volume or hæmatocrit reading, and a plasma protein whose percentage is unchanged although a reduction of the total quantity of protein in circulation has occurred. If this hæmoconcentration is corrected by glucose saline alone, the plasma protein level will fall as the blood volume rises. However if both glucose saline and plasma are given it can be maintained at the normal level.

This is of great clinical importance, and in my opinion a plasma transfusion should be given to every patient whose peritoneal infection is sufficiently severe to require an intravenous infusion. For, not only will it prevent the onset of the peripheral circulatory failure from which these patients may die, but if given in sufficient quantity it may even correct established peripheral circulatory failure in an apparently moribund patient.

Another and very important aspect of such plasma transfusions is that, provided the function of the heart remains satisfactory, pulmonary œdema is less likely to occur than with a glucose saline infusion. For the colloid osmotic pressure of the blood is maintained at the normal level, which pressure will oppose the passage of fluid from the blood-stream into the pulmonary alveoli.

During the past three years I have treated 31 patients with established general peritonitis on a post-operative regime of gastro-intestinal aspiration, plasma transfusion, glucose saline infusion, parenteral penicillin, and chemotherapy with a sulphonamide. Of these 31 patients, 25 were treated before signs of peripheral circulatory failure had occurred, and each patient received an average of 2 pints of plasma and 4 pints of glucose saline a day until intestinal activity was re-estabpatient who is a thoroughly bad risk by reason of bronchitis or cardiac weakness it may be preferable to try expectant treatment, and that gastric suction is a valuable safeguard in such a case, but in the average patient with early surgical closure under spinal anæsthesia, the mortality is negligible. Except for one case who had perforated five days and had a subphrenic abscess, I have not lost a patient with a perforation in the last 24 operated on in private. In my Unit during the past five years we have had 100 acute perforations with 8 deaths, but all these deaths were either in patients who had perforated over twenty-four hours before admission (2 cases) with very copious escape of fluid, or, if early, were bad risks by reason of chronic bronchitis and emphysema or old age.

My main contention is that by Hermon Taylor's method, it is impossible to be sure that the gastric suction is preventing the escape of duodenal contents into the peritoneum in dangerous amounts. The stomach may be sucked dry, but a stenosis or spasm at the pylorus may so shelter the perforation in the duodenum from the effect of the suction, that bile and duodenal contents pour out in lethal quantities. And we know that although this fluid may be sterile at first, it soon becomes infected, and the peritonitis may go on to fatal paralytic ileus. One feels little anxiety about an early perforated ulcer that has been closed securely by suture, but I could not sleep at night if I were wondering to what extent leakage might be going on under the gastric suction régime. I believe expectant treatment is only justified in bad-risk cases, and for them it is a definite advance in surgical technique. Hermon Taylor states that the orthodox surgical practice is to suture the perforation and *drain the peritoneum*, but surely drainage for these cases has been abandoned as being both unnecessary and dangerous.

REFERENCES

CRILE, G., Junior (1946) *Surg. Gynec. Obstet.*, 83, 150.
FAULEY, G. B., DUGGAN, T. L., STORMONT, R. T., and PFEIFFER, C. C. (1946) *J. Amer. med. Ass.* 126, 1132.
HUDSON, R. VAUGHAN, and SMITH, R. (1941) *Lancet* (i), 438.
SPALDING, J. E. (1946) *Lancet* (ii), 250, 643.
TAYLOR, HERMON (1946) *Lancet* (ii), 251, 441.
YOUNG, J. F., and COLE, WARREN H. (1946) *Arch. Surg.*, 53, 182.

Mr. C. G. Rob: *Protein balance in acute peritonitis.*—Recovery from established acute general peritonitis whilst it is dependent to a certain extent upon the skill of the operating surgeon, is governed to a far greater degree by the pre-operative and post-operative care which the patient receives. I intend therefore to discuss one factor in the ward care of these patients. This factor is protein balance.

During the late war surgeons were interested in protein balance, and a large amount of research was undertaken with particular reference to protein metabolism in wound healing, burns, and wound shock. Amongst these investigations the easily estimated plasma proteins received considerable attention, and some surprising facts came to light. For example the patient with chronic long-standing wound sepsis usually has a normal plasma protein, although a very considerable total loss of protein has occurred; presumably the blood protein level is kept up at the expense of the tissue proteins. However, in acute diseases such as burns or acute peritonitis the plasma protein level may fall before the tissue proteins can be mobilized to replace the loss.

Patients with acute general peritonitis suffer from a reduction of the body protein, which progresses with the disease until it becomes apparent as a fall in the plasma protein level. This reduction of the body protein occurs in four main ways:

(1) As exudate from the surface of the inflamed peritoneum which surface is equal to the cutaneous surface of the body. (2) Into the lumen of the distended intestine when paralytic ileus has occurred. (3) Into the serous and subserous layers of the peritoneum due to vasodilatation and inflammatory œdema. (4) Due to an associated reduction of protein digestion.

Section of Ophthalmology

President—Harold Levy, F.R.C.S.

[*October* 10, 1946]

Denig's Operation for Trachoma: Two Cases.—Noah Pines, M.B.

Dr. Pines demonstrated a man aged 73, with a gross pannus trachomatosus of the left eye from which he had suffered for over six years. Pines saw him first at the London Jewish Hospital ten days ago and intends to perform Denig's operation on the eye.

The other case was a woman aged 55, who twelve years ago presented a similar picture on her right eye and was operated at the same hospital. Denig's operation proved to be successful and the cornea since then remains clear; the eye quiet. The transplanted mucosa of the lip is still intact from 9 o'clock to 3 o'clock.

Usually the reported cases in the literature were observed for one to three years and this is one of the longest so far reported.

Denig (1911) operated first in 1910, following the work of Ichikawa, who proved the continuity of trachoma from fornix through the conjunctiva bulbi and so to the cornea. He transplanted first the conjunctiva of the healthy eye, but soon changed to the mucosa of the lip. In the first few years he performed 42 operations with 8 recurrences and failure of the mucosa to heal up on the eye in 5 cases. Ogata in 1930 saw good results from the operation in 95 cases. L. Pines in 1931 reported his results in 406 cases, with no improvement in 42 and recurrences in 16. The ætiology of pannus—by continuity or by contact—is still debated. Parsons (1942) is against the continuity, and so is Fuchs (1933). Wolff (1944) and Duke-Elder (1938) hold that there is a simultaneous infection of the cornea and conjunctival fornices. Prokrowsky and Taborisky (1914) (Ophthalmological Congress, Moscow, 1913) were partisans of continuity. A new point of view is brought in by Filatoff (1945) who ascribed the good result of the operation to the stimulant effect of transplanted mucosa. He even implants under the conjunctiva bulbi a belt from the pieces of sclera, taken from a cadaver, preserved for a few days, at the temperature of 4° C., and claims good results. He is also favourably impressed by the result of the operation. Indications for the operation are very few. The chief one is the intractable pannus and pannus crassus. On the whole, MacCallan is right, that usually pannus improves with the general improvement of the trachoma.

REFERENCES

Denig, R. (1911) *Z. Augenheilk.*, 25, 278.
Duke-Elder, W. S. (1938) Textbook of Ophthalmology. London, p. 1609.
Filatoff, V. P. (1945) Optical Transplant of the Cornea. Odessa.
Fuchs, E. (1933) Diseases of the Eye. London, p. 78.
Ichikawa, K. (1910) *v. Graefes Arch. Ophthal.*, 73, 303.
Parsons, J. H. (1942) Diseases of the Eye. London, p. 178.
Prokrowsky and Taborisky (1914) *Klin. Mbl. Augenheilk.*, 52 (1), 548.
Wolff, E. (1944) A Pathology of the Eye. London, p. 29.

lished, the plasma being given as a prophylactic against a possible fall in the blood protein level and the resultant circulatory failure. Not one of these patients developed any sign of peripheral failure and all made a satisfactory recovery.

The remaining 6 did not receive a plasma transfusion until after peripheral circulatory failure had developed, they were moribund with a very rapid thready pulse, a subnormal temperature, a cold clammy skin, and a clear mentality. But in spite of this 3 recovered, their recovery being due I have no doubt to the very large quantities of plasma which they received. Total volume of plasma which each patient received was spread over several days, and consisted of an initial large and rapid plasma transfusion of 4 to 8 pints, followed by an average intravenous fluid intake of 6 pints per day including a maintenance dose of plasma. Feeding by mouth was restarted as soon as the abdominal condition would allow.

In conclusion, whilst the vast majority of patients with acute peritonitis recover without the aid of a drip or suction, the minority with acute generalized peritoneal inflammation need all the help that we can give them, if they are to get better.

These seriously ill patients lose a great quantity of protein, which loss can only be corrected by the intravenous route. I therefore recommend that every patient whose peritonitis is so bad that an intravenous infusion is necessary, receives plasma as a prophylactic measure against the peripheral circulatory failure from which these patients so often succumb, and that the moribund peritonitis patient with a rapid thready pulse and cold clammy skin is given a chance by energetic plasma transfusions. For patients up to middle age the results may be dramatic.

See ELMAN, R. L., LISCHER, C. (1943) *Internat. Abstr. Surg.*, 76, 503.

Mr. R. Vaughan Hudson: *Prophylactic use of sulphonamides.*—Collier and Jackson have shown that after the implantation of an intraperitoneal sulphonamide, the concentration in the portal vein was three to four times that of the blood-stream. This observation produced evidence that toxins and bacteria from the general abdominal cavity were conducted by this route, and reaffirmed our surmise that a great deal more was happening in the hepatic and renal tracts than could be deduced from examination of the systemic blood-stream.

Parenteral penicillin.—One had at first regarded penicillin in the light of closed lesions which had occurred within the intact peritoneal cavity, and failed to appreciate that where an injury had occurred from the outside pyogenic organisms were swept in with the missile; surgical incision can be regarded in the same light, and prolonged drainage also invites the entry of pyogenic organisms.

In this respect penicillin is proving to be most successful in preventing secondary infection of the surgical incision, and secondary infection of essential drainage-tube sites. Moreover, its great value is in the prevention, or control, of the thoracic complications so commonly occurring in the surgery of acute abdominal lesions. This latter is particularly gratifying as sulpha-therapy has been so disappointing in the prevention and treatment of these pulmonary lesions.

Perforated ulcer.—I have had five cases of perforated ulcer in which the patient has refused surgery but has recovered. The interesting factor was the typical complication of post-perforative basal collapse and pneumonia which gave rise to great anxiety in convalescence.

Suction drainage.—I feel that Hermon Taylor has made us appreciate still more the value of suction drainage, and whether the surgeon decides upon non-operative, or operative measures, it is suction drainage that will prove to be the essential factor in reduction of mortality.

Lastly, I wish to emphasize the extreme importance of diagnostic straight X-rays of the abdomen, and their great value in the post-operative management of the physiological recovery of the alimentary tract.

or silkworm gut. The stitches were tied up and the shield put over it, and at the end of a week the stitches were cut.

Sir Stewart Duke-Elder said that Mr. Williamson-Noble was to be congratulated on a successful result of a complicated operation. He had seen quite a number of these devices for artificial eye implants of which there were all sorts of modifications. As far as he could make out this was one of the most satisfactory. One difficulty, however, which had been met with was that after a considerable time—something like eighteen months or two years—some of these plastic implants began to excite a reaction and become loose. Perhaps in these cases the plastic used was of an irritating type. In the Army a plastic implant was used to a considerable extent, but some difficulty was experienced in getting a material which did not cause a reaction. In America instead of a plastic, tantalum had been recently used—a metal which was entirely inert to the tissues. As far as could be seen—they had not been using it for very long—there was much less reaction with tantalum, and, theoretically at any rate, it should be better than an unsuitable type of plastic over a long time. The great drawback to all these operations was the length of time taken. He did not know how long Mr. Williamson-Noble took over the implant.

Mr. Williamson-Noble: About thirty-five minutes.

Sir Stewart Duke-Elder said that the time was shorter than in those cases of which he had had experience.

Mr. Williamson-Noble added that Mr. Hamblin had made an implant for him which was very good and was hoping to produce them in quantity. Mr. John Weiss had produced some differently coloured threads in silk.

The President: Could you use catgut ?

Mr. Williamson-Noble: It might be possible, but there would be more reaction with it. There was very little reaction after this operation.

[*November* 14, 1946]

Ophthalmo-neurological Symptoms in Malignant Nasopharyngeal Tumours. [*Summary*[1]]

By Erik Godtfredsen, M.D.Copenhagen

Malignant nasopharyngeal tumours, though rather infrequent, are by no means rare. Over 2,000 cases have now been published in the literature. Personally, I collected 454 cases over a period of ten years from four Scandinavian radiological clinics: Radiumhemmet, Stockholm and the Radiological Clinics of Lund, Copenhagen and Aarhus, which together serve a population of 7½ million people. The frequency of malignant nasopharyngeal tumours constituted 1% of the total number of cancer cases, i.e. a frequency of the same relative magnitude as that of choroidal melanosarcoma.

As, however, only the cancer cases that are likely to respond to irradiation are referred to the radiological clinics, a correction must be made for this percentage to ascertain the frequency among the total number of cancer cases in the population. The figure then arrived at is 0·4% of all cases of cancer.

The frequency figures for each year show a definite rise in the annual number of cases in the course of the decade in question (a rise of about 40 cases yearly).

38% of the patients presented ophthalmo-neurological symptoms.

Histopathological examinations revealed both carcinomas and sarcomas, in conformity with the fact that malignant nasopharyngeal tumours arise from the mucous membrane and the lymphatic tissue in the nasopharynx.

Age-incidence.—All age-classes from 4 to 79 were represented, but half of the patients were found within the age-classes of 41 to 60. One-fourth of the patients were 40 years of age or younger.

For no discoverable reason there were twice as many men as women.

Symptomatology of Malignant Nasopharyngeal Tumours [454 Cases]

There are four well-defined groups of symptoms: (1) Ophthalmo-neurological symptoms due to the infiltrative growth of the primary tumour or its metastases

---

[1] To be published in full, *Brit. J. Ophthal.*, 1947.

(a) Diabetic Cataract; (b) Endocrine Cataract.—A. LISTER, F.R.C.S.

(a) Mr. Lister said that the first of these cases was a woman aged 36. For several years she had suffered from thirst and polyuria. She had been attending London Hospital since June 1944 for diabetes. In 1944 the sugar tolerance test showed fasting blood sugar, 332 mg. per 100 c.c.; ¾ hour, 400 mg. per 100 c.c., and 2 hours 364 mg. per 100 c.c. She had been on insulin since first attending. On examination both eyes were healthy apart from the following changes in the lenses: between the zone of disjunction and the surface of the adult nucleus at the front and back of the lens (i.e. throughout the cortex) were numerous small whitish-grey opacities interspersed with iridescent particles, some of which were coloured. The nuclei were clear; the fundi were normal, and the vision in each eye was 6/24.

(b) The other case was a patient aged 55, in whom the diagnosis was cataract due to endocrine disturbance. The patient had been attending the London Hospital for some months with glycosuria, which was controlled by diet. There were no other abnormalities apart from obesity. The family history showed that four sons were alive and well, and brothers and sisters were well. The mother had bad eyes.

On examination of the patient both eyes were normal except again for certain lens changes. Between the zone of disjunction and the nuclear surface were numerous opacities varying in size and shape. The large ones were best described as snowflakes, of which there was an accumulation at both posterior poles. The smaller opacities were, many of them, coloured and gleaming. Vision was 6/36 in each eye.

In some comment on both these cases Mr. Lister said that they showed points of similarity to each other and to other conditions in which there was endocrine disturbance of some kind. Mr. Goulden had described a number of such cases (1928, *Trans. ophthal. Soc. U.K.*, **48,** 97). The points of similarity and the points which distinguished these cases from senile and pre-senile forms of cataract were: (1) The appearance of the opacities; some being large and white, and others small, iridescent, and coloured; (2) their distribution, which was throughout the cortex; and (3) the freedom of the nuclei from opacities.

The first case was, he thought, a true diabetic cataract. Although diabetes and cataract were often associated, the cataract was, in the vast majority of cases, senile in type, and the association probably coincidental, but occasionally diabetic cataract similar to the one he was discussing was seen. He was doubtful about the other case. The patient was older—she was 55—and the opacities were larger than were found in true diabetic cataract. She was obese and had a slightly myxœdematous appearance. He would suggest that in her case the lens changes were due to myxœdema.

Plastic Implant into Socket.—F. A. WILLIAMSON-NOBLE, F.R.C.S.

This was a case of an operation for enucleation described by Cutler (1946, *Arch. Ophthal.*, **35,** 71) and adopted by the U.S.A. Medical Service. The plastic implant was designed to promote the fitting of a glass eye or plastic eye into the cavity. In appearance the plastic implant was rather like a small wastepaper basket. By means of a series of epidiascope pictures Mr. Williamson-Noble illustrated the stages of insertion. The stitching material with two needles was threaded through two holes at the bottom, and then up through the 12 o'clock and 6 o'clock positions. Two other sets of sutures were inserted, and the threads brought through a lucite stud, so that when they were tied, the conjunctiva was carried by the stud into the concavity of the basket. In view of the complexity of the suturing, it was desirable to use stitches of different colours. He thought it was an improvement on the ordinary glass or gold ball. He had found it best to use some sort of nylon trigeminus are found in practically all cases. There is a change in frequency between eye nerve lesions and trigeminus lesions at the three stages of the disease.

TABLE II.—INCREASE IN FREQUENCY (%) OF OPHTHALMOLOGICAL SYMPTOMS COMPARED WITH THAT OF TRIGEMINUS LESIONS—FROM THE FIRST SYMPTOM TO THE FULLY-DEVELOPED PICTURE.

	1st symptom 11 months before diagnosis is made %	Initial picture 4 or 5 months before diagnosis is made %	Fully developed picture when the diagnosis is made %
Frequency of ophthalmological symptoms ..	14·4	51·0	75·2
Frequency of trigeminus lesions	71·0	70·0	68·0

Table II shows that the purely ophthalmological complaints constitute a small percentage of the first symptoms, while the trigeminus lesions are in great majority. But at the second stage of the analysis (four or five months before the diagnosis is made) the ophthalmological symptoms increase very considerably, being now found in half of all the cases, whereas the percentage of trigeminus lesions has hardly changed. The increase in the frequency of ophthalmological symptoms continues—though less abruptly so—up to the point of time at which the diagnosis is made, comprising by that time 75·2% of the cases. They are then more frequent than the trigeminus lesions, which remain at a stationary level 68%.

It should therefore be possible to diagnose these cases without waiting for the appearance of the later symptoms. The first symptom—occurring about ten or eleven months before the diagnosis is made—is usually (71·0%) trigeminal neuralgia in the maxillary area. This may be combined with either nasal stenosis, metastatic cervical glands or tubal occlusion. The only ophthalmological symptom at this stage is abducens paresis; there is no other symptom.

By the time of the second analysis—four or five months before the diagnosis is made—there is not only a quantitative, but also a qualitative increase in the purely ophthalmological symptoms. There are no essential qualitative differences between the ophthalmological symptoms of the second and third stages. The purely monosymptomatic ophthalmo-neurological cases are few (3%) at this stage, since forms combined with rhinological or otological symptoms and metastatic cervical glands respectively are found in 40% each of the cases.

Accordingly a patient who at this stage of the disease applies to an ophthalmologist on account of eye muscle paresis, visual disturbances, or exophthalmos, with or without trigeminal neuralgia, will present symptoms also from the other main groups mentioned here. When the ophthalmologist is consulted by patients suffering from abducens paresis, impairment of vision, exophthalmos, or Horner's syndrome he should always suspect a malignant nasopharyngeal tumour. Palpation for metastatic cervical glands, and questioning as to rhinological or otological symptoms, and possibly an oto-rhinological special examination will help to confirm the diagnosis.

TABLE III.—NATURE AND FREQUENCY OF OPHTHALMO-NEUROLOGICAL SYMPTOMS IN 172 PATIENTS WITH MALIGNANT NASOPHARYNGEAL TUMOURS.

Eye symptoms 129 patients 75·2%	Alone 40 patients 23·4%	Ophthalmoplegia..	22 patients
		Ophthalmoplegia + II	11 patients
		Ophthalmoplegia + Horner ..	3 patients
		II-lesion alone	2 patients
		Exophthalmos	2 patients
	With V-lesion 44 patients		25·6%
	With other cranial nerve-lesion, partly V. 45 patients		26·2%
V-lesions 117 patients 68·0%	With eye symptoms 78 patients		45·4%
	Without eye symptoms 39 patients		22·6%

into the base of the skull and adjacent regions; (2) rhinological and (3) otological symptoms due to the exophytic growth of the primary tumour into the nasopharynx affecting the Eustachian tube; (4) enlarged cervical glands from lymphogenous metastases.

The early symptoms are important.

The first analysis covers the first symptom(s) observed by the patient. This appears on an average eleven months (three or four years at most) before the exact diagnosis is made.

The second analysis covers the initial signs and symptoms in a wider sense. At this stage there are several symptoms within one group, or different groups are represented. This pathological picture is seen on an average four or five months before the exact diagnosis is made.

The third analysis covers the fully developed picture, and corresponds to the time at which the diagnosis is made and the patient referred to a radiological clinic.

The percentage frequency of ophthalmo-neurological symptoms in these three analyses appears from Table I, which also shows the frequencies of the three other main groups of symptoms.

TABLE I.—PERCENTAGE DISTRIBUTION OF THE DIFFERENT GROUPS OF SIGNS AND SYMPTOMS AT THREE STAGES OF THE DISEASE AMONG 454 CASES OF MALIGNANT NASOPHARYNGEAL TUMOUR.

	1st symptom 11 months before diagnosis is made	Initial picture 4 or 5 months before diagnosis is made	Fully developed picture when the diagnosis is made
	%	%	%
Ophthalmo-neurological symptoms	16·0	34·8	38·0
Rhinological symptoms	30·8	51·4	56·2
Otological symptoms ..	23·0	48·5	49·1
Metastatic cervical glands	32·6	48·4	74·9

Table I shows that ophthalmo-neurological complaints appear as the first symptom in 16·0% of the cases, while metastatic cervical glands and rhinological symptoms are both present as the first symptom in about one-third of the patients. Otological symptoms are rarer, being present in about one-fifth of the cases only. Nearly all the cases are monosymptomatic at this stage of the disease (in nine-tenths of the cases); and it must be emphasized that two-thirds of the patients did not complain of nasal symptoms.

Second analysis: The most conspicuous changes at this stage are as follows: The ophthalmo-neurological symptoms have more than doubled in frequency, occurring now in 34·8%, whereas the other groups of symptoms present more moderate increases in frequency, each being found in half of the patients. The frequency of monosymptomatic cases has become reduced to one-fourth.

Third analysis: There are two facts which are particularly noteworthy: First the frequency of ophthalmo-neurological symptoms is almost stationary, being found in a total of two-fifths of the cases (or 38·0%), and secondly there is a considerable increase in the frequency of metastatic cervical glands, which are now present in three-fourths of the patients. Oto-rhinological symptoms, on the other hand, are stationary, occurring in about half of the cases.

These analyses show plainly that when ophthalmo-neurological symptoms do occur they appear early in the disease, and they can be sorted out as a special group four or five months before the exact diagnosis is made. They do not—as was hitherto believed—appear only at the advanced and hopeless stage.

NATURE AND FREQUENCY OF OPHTHALMO-NEUROLOGICAL SYMPTOMS

All forms of cranial nerve lesions are met with, as might have been expected from the manner of growth of the tumour. Lesions of the eye nerves and/or

TREATMENT

The treatment of malignant nasopharyngeal tumours is now purely radiological, as there is contra-indication for operative treatment (both from a technical and from a biological point of view) of such deep-seated and invading tumour forms. Fortunately such tumours are generally rather radiosensitive on account of their biologically immature character.

A strong, external, protracted, fractional X-ray or teleradium treatment is given, which on rare occasions is supplemented by a local radium or X-ray treatment. The X-ray treatment is given in anterior and lateral portals in doses of from 4,000 to 10,000 r during from three to eight weeks. This treatment can secure a lasting freedom from symptoms (over five years), but whether it does so depends to a certain extent on the histopathological type of the primary tumour and on the extent of the disease. The radiosensitive reticulum-cell sarcomas, for instance, show a "five-year cure rate" of nearly 40%, while the corresponding figure for the total number of cases amounts to 22·2%.

REFERENCE

GODTFREDSEN, ERIK (1944) Ophthalmo-neurological Symptoms in Malignant Nasopharyngeal Tumours. Copenhagen.

The Diagnosis and Treatment of Tumours of the Nasopharynx

By E. D. D. DAVIS, F.R.C.S.

TUMOURS of the nasopharynx are difficult and unsatisfactory to treat but fortunately they are comparatively rare. I have studied the notes of 33 of my patients and the literature of a large number of other cases with the object of establishing an earlier diagnosis and more successful treatment. The 33 cases were seen during the past twenty-five years and consisted of: Carcinoma, 19; lympho-sarcomata or lymphomata, 4; angio-fibromata, 9; myxosarcoma of doubtful origin, 1.

These are the types of tumours recorded by other observers but some call the fibroma or angio-fibroma a fibro-sarcoma. Two of the angio-fibromata proved to be sarcomata and recurred some time after removal. This list does not include rare tumours such as ameloblastomas or adamantinomas which extend from the pituitary body along the craniopharyngeal canal or from the maxillæ into the nasopharynx.

The early diagnosis of tumours of the nasopharynx is delayed because they are hidden in a cavity which is sometimes difficult to inspect. This inspection of the nasopharynx in patients who cannot tolerate the small mirror placed behind the soft palate is difficult and also in advanced cases of carcinoma when inability to open the mouth and fixation of the mandible is a symptom. Moreover the patient does not consult a doctor until the growth is large enough to produce a series of mechanical signs which are slow and insidious in onset and when it is too late for successful treatment. Malignant growths within themselves do not produce any specific diagnostic symptoms or signs. Blood changes, cachexia, &c., are of no practical value in the early diagnosis. Gordon New of the Mayo Clinic reported 79 cases of malignant growths of the nasopharynx; 34 were epitheliomata and 33 were lymphosarcomata. Of these 79 patients 74 had had an operation for the relief of symptoms without recognition of the fact that a primary growth in the nasopharynx was the cause of these symptoms. In 24 patients tonsils and adenoids had been removed, in 18 glands in the neck, in 12 the wisdom or third molars had been extracted. Various intranasal operations had been performed in 19 and finally a mastoid operation for the relief of pain.

The symptoms and signs of carcinoma of the nasopharynx vary with the site and type of growth and the commonest site is the lateral wall. When the growth

Table III shows that 75·2% of the cases had ophthalmological symptoms, and that two-thirds of these patients presented trigeminus lesion as well. Correspondingly two-thirds of the 68% with trigeminus lesion presented ophthalmological symptoms as well. It appears from this close connexion between ophthalmological symptoms and trigeminus lesion that the tumour tissue usually affects the area round the cavernous sinus, where—as already mentioned—these cranial nerves run in intimate relation to each other.

The cases with ophthalmological symptoms can be divided into: (1) Purely ophthalmological cases; (2) forms combined with trigeminus lesions; and (3) forms combined with trigeminus lesions together with other cranial nerve lesions, usually lesions of the ninth and tenth nerves.

TABLE IV.—NATURE AND FREQUENCY OF 461 SINGLE NERVE LESIONS IN 172 PATIENTS WITH MALIGNANT NASOPHARYNGEAL TUMOURS.

Nerve lesions	VI	III	IV	II	Horner	V	Others
Frequency	114	42	29	29	27	119	101
%	24·0	9·1	6·3	6·3	5·8	25·7	21·8

It appears from Table IV that eye nerve lesions constitute more than half of the total number of cranial nerve lesions, partly in the form of ophthalmoplegias (39·4%), partly as visual pathway lesions (6·3%), and Horner's syndrome (5·8%). Among the ophthalmoplegias the predominating group is that of paresis of the sixth cranial nerve, which constitutes nearly one-fourth of the total number of nerve lesions, being thus almost equal in frequency to trigeminus lesions, 25·7%.

Pareses of the third and fourth cranial nerves are of much rarer occurrence. The same is the case with pareses of the other cranial nerves (seven, and nine—twelve), which altogether constitute 21·8% distributed over 7 cranial nerves, chiefly the bulbar nerves.

Of the 461 cranial nerve lesions 6·7% were bilateral lesions, which in practically all cases affected the eye nerves. The eye symptoms therefore play a predominant part in the early diagnosis of malignant nasopharyngeal tumours.

The ophthalmoplegias generally manifested themselves as massive paralyses with associated clinical findings. The visual pathway lesions, on the other hand, presented various degrees of severity from a slight impairment of vision to the more frequent total amaurosis with atrophy of the optic nerve or choked disc. Quadrantanopia or hemianopia was of rarer occurrence.

Exophthalmos due to penetration of the tumour into the orbit was found in 19 patients with varying degrees of chemosis and disturbances of motility, generally associated with a poor general state.

The trigeminus lesions are usually neuralgias in one or more of the three branches; the motor root is more rarely affected.

There are multiple cranial nerve syndromes in many of the cases. For example there is one cranial nerve syndrome with ophthalmoplegia (most often sixth nerve paresis) and paresis of the twelfth cranial nerve and usually also trigeminal neuralgia which merits particular attention. As this syndrome was observed in 9 cases, it was scarcely an accidental combination. The ophthalmoplegia and the trigeminal neuralgia are the result of tumour invasion round the cavernous sinus. The paresis of the twelfth cranial nerve, which was present without lesion of other distal cranial nerves (so that diffuse tumour growth can be excluded) is a result of involvement of the lymphatics. Metastatic cervical glands were observed in all these cases, and the primary tumour was often situated on the lateral wall of the nasopharynx so that the enlarged retropharyngeal lymph glands, which lie off the hypoglossal canal, compressed the nerve.

This cranial nerve syndrome is thus conditioned partly by the intracranial growth of the primary tumour, and partly by lymphatic metastases, and is therefore pathognomonic of a malignant neoplasm in the nasopharynx.

All the 19 cases mentioned above derived little benefit from radium or deep X-ray therapy and all of them died from twelve to eighteen months from the first appearance of symptoms. Radium was most unsatisfactory because it caused considerable reaction with pain and irritation of the mucosa and was followed by metastasis. The lymphosarcomata and the lympho-epitheliomata disappeared rapidly with radium treatment but they all died of metastases within two years. However deep X-ray therapy is the only treatment which holds out any hope of success or even relief.

The bleeding fibroma of male puberty is benign and occurs in boys between the ages of 10 and 20. It is a sessile hard globular fixed tumour usually growing from the body of the sphenoid and basi-occipital bone or from the inaccessible roof of the posterior nares. The rate of growth of this tumour varies considerably and it may become so large as to encroach on the antrum, the posterior ethmoidal cells or sphenoid and by pressure produce optic atrophy and loss of sight. At a later stage the tumour broadens the bridge of the nose, displaces the eyeballs forwards, then outwards. At first one eye is displaced and then the other. The result is known as "frog-face". It is very difficult to distinguish this fibroma from a malignant fibro-sarcoma. The sarcoma grows very rapidly, it is softer, not circumscribed, often occurs at a later age. It ulcerates, bleeds spontaneously and also produces the deformity of "frog-face". The histological section shows larger ill-defined blood spaces and many more round cells than the fibroma but diagnosis by the section is not infallible. [Section of fibroma and of fibro-sarcoma shown.] I have come to the conclusion that if a "fibroma" which has been completely removed by enucleation recurs it is probably a sarcoma. In my experience radiotherapy has no beneficial effect on the fibroma or fibro-sarcoma but Figi of the Mayo Clinic has treated a number of cases of fibroma with diathermy and radium implantation with success.

BIBLIOGRAPHY

BAYON, P. G. E. (1907) *Brit. med. J.* (ii), 1400.
DRUMMOND, W. A. D. (1939) *Proc. R. Soc. Med.*, **32**, 200.
FIGI (1940) *J. Amer. med. Ass.*, **115**, 665.
—— (1940) *Coll. Pap. Mayo Clin.*, p. 835.
MILLIGAN, W. (1924) *J. Laryng. Otol.*, **39**, 537.
NEW, GORDON (1922) *J. Amer. med. Ass.*, **79**, 10.
—— (1920) *Coll. Pap. Mayo Clin.*, p. 1160.
TILLEY, H. (1903) *J. Laryng. Otol.*, **18**, 45.

Sir Stewart Duke-Elder said that so far as he knew the literature of the subject, this collection of 454 cases of these rare tumours was by far the largest extant; the only one approaching it—and that a very much smaller collection—derived from the Mayo Clinic. This work was not only a compliment to Dr. Godtfredsen's industry, but also to the medical system of the northern countries, which, although small, were able to surpass in this respect not only our own land but even America with all its efficiency. From his own standpoint the most interesting thing was that 38% of these cases should have shown ophthalmological symptoms, and the interest became really acute when he learned that in 16% the first signs were ophthalmological. It was certainly a disturbing thought that in these conditions, which were often forgotten by the ophthalmologist, the responsibility for early diagnosis which might well be a question of life or death to the patient, was so often primarily ophthalmological. Only that morning he had received a letter from a doctor in Scotland stating that a patient whom he had seen six months ago suffering from an abducens palsy was now showing signs of what the speaker supposed was an advanced and untreatable nasopharyngeal tumour; if he had had the advantage of hearing Dr. Godtfredsen's paper before he saw the case six months ago, he would have been more alive to this possible development. If only for that reason this paper was one of the most important that they had listened to this session.

Mr. D. V. Giri said that Mr. Davis had suggested that the differentiation between a sarcoma and a fibroma was not easily made, and in fact that it could only be established as sarcoma if, after removal, there was a recurrence. But when a section of the tumour was made and examined did it not reveal the nature of the growth ?

Mr. E. D. D. Davis, in reply to Mr. Giri, showed two microscope sections, one of a fibroma and the other of a sarcoma. The sarcoma showed that the blood spaces were not so well is in the region of the Eustachian tube or lateral wall the first symptom may be a unilateral deafness with fluid in the middle ear as the result of Eustachian obstruction. This is known as the auricular type of growth and it was the first symptom and sign in 3 of my 19 cases. Sometimes a diagnosis had not been made until secondary growths appeared in the cervical lymphatic glands. The glandular type of case shows the enlargement of the deep cervical lymphatic glands at the angle of the jaw on both sides of the neck or the superficial cervical group of glands along the posterior border of the sternomastoid.

This was the first sign in 6 cases. This is the type of case for which tonsils had been enucleated or a dissection operation for glands in the neck had been performed before the diagnosis of carcinoma of the nasopharynx had been made. The enlargement of the lymphatic gland is the first sign of a lympho-epithelioma or lymphosarcoma.

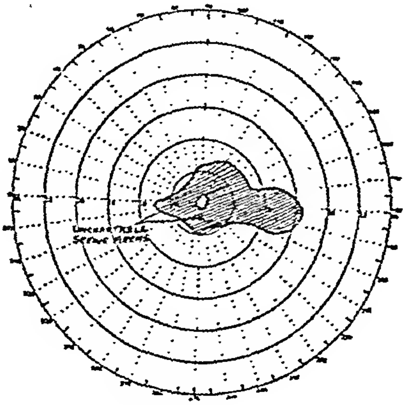
Neurological symptoms such as headache, pain, diplopia and paralysis of cranial nerves, particularly the sixth cranial nerve were the first symptoms in 6 cases. These patients are seen first by the ophthalmic surgeon or neurologist and the primary pharyngeal lesion may escape detection. The headache is bi-temporal or on the vertex of the skull. A neuralgia of the fifth cranial nerve or upper cervical spinal nerves is occasional but otalgia and pain in the distribution of the auriculotemporal nerve are more common. Paralysis of the sixth cranial nerve first on one side and then on both is the commonest. It is followed by ptosis and paralysis of the third nerve and later a complete ophthalmoplegia on the one side and a partial on the other. There is evidence to show that this growth may commence in the body or great wing of the sphenoid and later burrow to the surface in the nasopharynx particularly when a paralysis of a cranial nerve is the first sign and precedes the other symptoms by some weeks. An infrasellar pituitary tumour may resemble a carcinoma of the nasopharynx but pituitary tumours more often produce a bi-temporal hemianopia and other localizing signs.

The superficial lymphatic glands along the posterior border of the sternomastoid are involved early and the removal and section of such a gland reveal a grade 3 or 4 carcinoma. Gordon New has recorded 2 cases of paralysis of the nerves in the jugular foramen with the resulting paralysis of the trapezius, sternomastoid, palate, pharynx and recurrent laryngeal nerve. The growth was found in the lateral wall of the nasopharynx and probably originated in the region of the jugular foramen. A persistent sore throat is said by some to be an early symptom.

Nasal symptoms especially epistaxis or a blood-stained mucous discharge from the nasopharynx accompanied by headache in a patient of cancer age is suspicious, and a careful examination of the nasopharynx with the post-nasal mirror, the endoscope passed through both nostrils alternately and with the finger, should be made. Good illumination and a direct view of the nasopharynx can be obtained by retracting the palate with a special coolite retractor or curved pencil torch. The nasopharynx thus illuminated can be clearly seen when looking through the anterior nares with a large nasal speculum. These methods of examination of the nasopharynx are essential to the early diagnosis of new growths of this area. An X-ray photograph which shows the extent of the growth is useful. Nasal obstruction except in cases of angio-fibroma is not common. When the growth is accessible as large a piece as possible should be removed for a biopsy. This can be done through the nose and the area should be sealed by a small diathermy electrode. Sometimes a metastatic lymphatic gland is more useful for a biopsy.

The treatment of malignant growths of the nasopharynx is confined to deep X-ray therapy. These cases are inoperable and beyond surgery when first seen. Deep X-ray therapy is more hopeful now that an earlier diagnosis is possible and the technique has improved.

of ring shape, with a central seeing island, and much improved visual acuity, and was kind enough to draw my attention to this; I had not seen the patient for six months; previously I had found the usual poor vision and large scotoma.



Sister D. 4/2000 W. July 25, 1946.

I examined her fully on July 25, 1946. The right pupillary reactions were ill-sustained, and the right disc pale. Vision was a full 6/5. There was no peripheral field loss, but the screen examination to 4/2000 showed a central ring scotoma, the seeing island being about 1° in size. There were also two unchartable seeing islands of much lower acuity, in the lower nasal part of the scotoma.

We have been able to find no reference to such development in a case of retrobulbar neuritis, and therefore considered it worthy of report. We attribute the result to recovery of a few central affected fibres, but the well-known vulnerability of the papillo-macular bundle makes the occurrence doubly interesting.

Dr. N. Pines said that he would explain the sudden blindness and the following restoration of the vision by angiospasm. He would suggest that the condition could be elicited by showing the difference in the retinal arterial tension between the right and left eyes.

Denig's Operation: Two Cases.—Noah Pines, M.B.

Case I.—Man aged 54. This case was one of trachoma chronicum cicatricum in which the tarsus of the left eye had been excised eighteen years previously; the incision having been made through the sulcus. The right eye was operated upon —Denig's operation—about twelve years ago, but the major middle part of the graft did not take. March 1944 the left eye showed keratitis pannosa ulcerosa.

January 15, 1946: There had been complete superficial corneal ulceration a week previously, but only the upper part of the cornea was then involved. It was a case of pannus trachomatosus.

January 29, 1946: The eye was better. July 23, 1946: Denig's operation was performed on the left eye, with satisfactory results.

Case II.—Man aged 73 with pannus trachomatosus crassus; previously shown on October 10, 1946.

October 18, 1946: Denig's operation was carried out.

The diagrams (*see* next page) reproduced from Professor Fillatoff's book "Optical Transplant of the Cornea," Odessa, 1945, illustrate the steps of the operation.

defined, and larger and there were many more round cells. A sarcoma often ulcerated and was much softer. Growth was very rapid and if an apparent fibroma recurred quickly after complete removal it was a sarcoma. The difference between the two sections was not conclusive and the diagnosis on the section only might be fallacious.

Sir Richard Cruise said that he had in mind a case which he had watched now for two months. The first symptom was exophthalmos, slight but definite, with retraction of the lid. In about a month the patient came again and he noticed some further development in the symptoms, paresis of outward and upward movements, and again when he came after two months. Were there tumours of this slow-growing character which would produce a slow increase of symptoms of this nature. X-ray photographs, stereoscopic, revealed nothing and an oto-rhinologist had seen the patient and could find nothing wrong with the sinuses. How long would it be possible for such a condition to go before anybody but a pharyngeal expert could decide that this was not a nasopharyngeal growth, or how soon could one expect a positive diagnosis of that nature to be made?

Mr. Lionel Colledge said that although Dr. Godtfredsen's paper had been most interesting, those who had studied the book he had written would realize that what he had given them that evening was only a small part of the knowledge of this subject which he had accumulated. He had attacked the matter on a broad front, and had made an even greater contribution to laryngology than to ophthalmology. His classification into four groups was very important, if only because it drew attention to the fact that only in one-third of the cases were local symptoms present in the early stages. He had also described the symptoms very elaborately, and he had described a syndrome of his own.

This form of disease was brought into prominence about thirty years ago by Trotter when he described a syndrome, later known as "Trotter's triad", in which there was depression of the palate, neuralgia in the lower divisions of the fifth nerve, and deafness. But Trotter described it in only 8 cases, and it only gave a very partial view of the subject, because there was a number of other important symptoms. In those days there was little to be done for the patients. If any operation could have succeeded it would have done so in Trotter's hands, but all his operative attempts were failures. The situation to-day was rather different. In at least 20% of the cases the tumour disappeared permanently on irradiation; in a far larger number it disappeared temporarily, but during the first year or two there were a number of recurrences, and even if there was no local recurrence, a good many of the patients succumbed to fresh deposits in bone, especially in the spine. It was rather an under-statement to say that about one in five gave a lasting good result.

Histological investigation of the problem showed that in this region about half the tumours were epiblastic and about half mesoblastic in origin, a much larger proportion of mesoblastic tumours than occurred in other parts of the body. In addition, many of the epiblastic tumours were classified as lympho-epitheliomas and undifferentiated carcinomas which responded well to radiotherapy. The highly differentiated epitheliomas gave very few good results, but their relative infrequency explained the good results of radiotherapy which was especially effective for lympho-epitheliomas, sarcomas and salivary gland tumours.

Dr. Godtfredsen, in reply, thanked all his colleagues in the Discussion. It had been most interesting to listen to Mr. Davis's experience. The histopathologic distribution was the same as that in his own material, but he (Dr. Godtfredsen) had not gone into the details of these questions in this paper. Sir Stewart Duke-Elder's case had similar features to many cases in his series, and if there had been time enough he could have described many difficult and tragic case histories.

In answer to Sir Richard Cruise he (Dr. Godtfredsen) said that in a small number of cases the primary tumour had a curious submucous mode of growth during a period from six to twelve months where it was impossible to see the tumour by post-rhinoscopic examination.

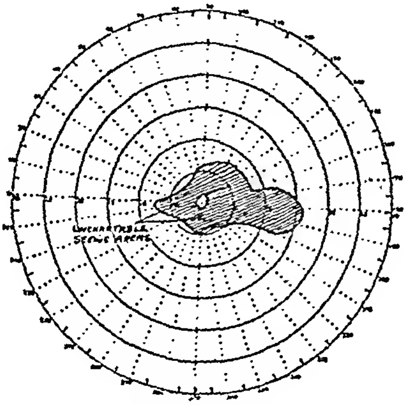
Ring Scotoma after Retrobulbar Neuritis.—FRANK W. LAW, F.R.C.S.

Patient in early middle age.

May 1942: Rapid loss of vision in the right eye; the signs pointed unmistakably to an acute retrobulbar neuritis, and neurological opinion (Dr. Behrman) found reason in the general examination and past history to confirm this diagnosis and attribute the cause to disseminated sclerosis. Vision was lost in five days and for ten days there was no perception of light; slow recovery occurred to counting fingers.

Past history.—She had an attack of vertigo seven years before she developed the neuritis. The attack lasted several days and was accompanied by ataxia for two weeks necessitating her staying in bed. Such a history, Dr. Behrman adds, is by no means uncommon in disseminated sclerosis.

The visual field was examined by Dr. Behrman on four occasions between 1942 and 1946, and the usual picture of a large central scotoma was found, with visual acuity to correspond. On the last occasion, however, he found the scotoma to be of ring shape, with a central seeing island, and much improved visual acuity, and was kind enough to draw my attention to this; I had not seen the patient for six months; previously I had found the usual poor vision and large scotoma.



Sister D. 4/2000 W. July 25, 1946.

I examined her fully on July 25, 1946. The right pupillary reactions were ill-sustained, and the right disc pale. Vision was a full 6/5. There was no peripheral field loss, but the screen examination to 4/2000 showed a central ring scotoma, the seeing island being about 1° in size. There were also two unchartable seeing islands of much lower acuity, in the lower nasal part of the scotoma.

We have been able to find no reference to such development in a case of retrobulbar neuritis, and therefore considered it worthy of report. We attribute the result to recovery of a few central affected fibres, but the well-known vulnerability of the papillo-macular bundle makes the occurrence doubly interesting.

Dr. N. Pines said that he would explain the sudden blindness and the following restoration of the vision by angiospasm. He would suggest that the condition could be elicited by showing the difference in the retinal arterial tension between the right and left eyes.

Denig's Operation: Two Cases.—NOAH PINES, M.B.

CASE I.—Man aged 54. This case was one of trachoma chronicum cicatricum in which the tarsus of the left eye had been excised eighteen years previously; the incision having been made through the sulcus. The right eye was operated upon —Denig's operation—about twelve years ago, but the major middle part of the graft did not take. March 1944 the left eye showed keratitis pannosa ulcerosa.

January 15, 1946: There had been complete superficial corneal ulceration a week previously, but only the upper part of the cornea was then involved. It was a case of pannus trachomatosus.

January 29, 1946: The eye was better. July 23, 1946: Denig's operation was performed on the left eye, with satisfactory results.

CASE II.—Man aged 73 with pannus trachomatosus crassus; previously shown on October 10, 1946.

October 18, 1946: Denig's operation was carried out.

The diagrams (*see* next page) reproduced from Professor Fillatoff's book "Optical Transplant of the Cornea," Odessa, 1945, illustrate the steps of the operation.

defined, and larger and there were many more round cells. A sarcoma often ulcerated and was much softer. Growth was very rapid and if an apparent fibroma recurred quickly after complete removal it was a sarcoma. The difference between the two sections was not conclusive and the diagnosis on the section only might be fallacious.

Sir Richard Cruise said that he had in mind a case which he had watched now for two months. The first symptom was exophthalmos, slight but definite, with retraction of the lid. In about a month the patient came again and he noticed some further development in the symptoms, paresis of outward and upward movements, and again when he came after two months. Were there tumours of this slow-growing character which would produce a slow increase of symptoms of this nature. X-ray photographs, stereoscopic, revealed nothing and an oto-rhinologist had seen the patient and could find nothing wrong with the sinuses. How long would it be possible for such a condition to go before anybody but a pharyngeal expert could decide that this was not a nasopharyngeal growth, or how soon could one expect a positive diagnosis of that nature to be made?

Mr. Lionel Colledge said that although Dr. Godtfredsen's paper had been most interesting, those who had studied the book he had written would realize that what he had given them that evening was only a small part of the knowledge of this subject which he had accumulated. He had attacked the matter on a broad front, and had made an even greater contribution to laryngology than to ophthalmology. His classification into four groups was very important, if only because it drew attention to the fact that only in one-third of the cases were local symptoms present in the early stages. He had also described the symptoms very elaborately, and he had described a syndrome of his own.

This form of disease was brought into prominence about thirty years ago by Trotter when he described a syndrome, later known as "Trotter's triad", in which there was depression of the palate, neuralgia in the lower divisions of the fifth nerve, and deafness. But Trotter described it in only 8 cases, and it only gave a very partial view of the subject, because there was a number of other important symptoms. In those days there was little to be done for the patients. If any operation could have succeeded it would have done so in Trotter's hands, but all his operative attempts were failures. The situation to-day was rather different. In at least 20% of the cases the tumour disappeared permanently on irradiation; in a far larger number it disappeared temporarily, but during the first year or two there were a number of recurrences, and even if there was no local recurrence, a good many of the patients succumbed to fresh deposits in bone, especially in the spine. It was rather an under-statement to say that about one in five gave a lasting good result.

Histological investigation of the problem showed that in this region about half the tumours were epiblastic and about half mesoblastic in origin, a much larger proportion of mesoblastic tumours than occurred in other parts of the body. In addition, many of the epiblastic tumours were classified as lympho-epitheliomas and undifferentiated carcinomas which responded well to radiotherapy. The highly differentiated epitheliomas gave very few good results, but their relative infrequency explained the good results of radiotherapy which was especially effective for lympho-epitheliomas, sarcomas and salivary gland tumours.

Dr. Godtfredsen, in reply, thanked all his colleagues in the Discussion. It had been most interesting to listen to Mr. Davis's experience. The histopathologic distribution was the same as that in his own material, but he (Dr. Godtfredsen) had not gone into the details of these questions in this paper. Sir Stewart Duke-Elder's case had similar features to many cases in his series, and if there had been time enough he could have described many difficult and tragic case histories.

In answer to Sir Richard Cruise he (Dr. Godtfredsen) said that in a small number of cases the primary tumour had a curious submucous mode of growth during a period from six to twelve months where it was impossible to see the tumour by post-rhinoscopic examination.

Ring Scotoma after Retrobulbar Neuritis.—FRANK W. LAW, F.R.C.S.

Patient in early middle age.

May 1942: Rapid loss of vision in the right eye; the signs pointed unmistakably to an acute retrobulbar neuritis, and neurological opinion (Dr. Behrman) found reason in the general examination and past history to confirm this diagnosis and attribute the cause to disseminated sclerosis. Vision was lost in five days and for ten days there was no perception of light; slow recovery occurred to counting fingers.

Past history.—She had an attack of vertigo seven years before she developed the neuritis. The attack lasted several days and was accompanied by ataxia for two weeks necessitating her staying in bed. Such a history, Dr. Behrman adds, is by no means uncommon in disseminated sclerosis.

The visual field was examined by Dr. Behrman on four occasions between 1942 and 1946, and the usual picture of a large central scotoma was found, with visual acuity to correspond. On the last occasion, however, he found the scotoma to be

Section of Psychiatry

President—Professor AUBREY LEWIS, M.D.

[*December* 10, 1946]

DISCUSSION: LEUCOTOMY AS AN INSTRUMENT OF RESEARCH

Dr. A. Meyer and Dr. T. McLardy: *Neuropathological studies* [*Abridged*].—Prefrontal leucotomy, in pursuing its therapeutic purpose, is furnishing us with a human experiment on the function of the frontal lobes on a scale comparable in its potentialities perhaps only with the first world war's head injuries which contributed such a wealth of new knowledge through the work of Head, Holmes, Goldstein and others.

The neuropathological (and neuro-anatomical) is of course only one among the many aspects of this experiment. Valuable opportunities of research are offered in many other fields including neurology, psychology and pharmacology. The neuro-pathological side of the problem is of some special importance because most, if not all, of the clinical research work would be largely invalid without ultimate pathological control.

The importance of pathological control is illustrated by the following table which shows both hemispheres in all our cases at present numbering 27, analysed in terms of the segments involved in the cut. It demonstrates clearly the variability of the lesions and that in only a few cases was the general aim attained of a bilateral lesion

SEGMENT CUT

Year of opn.	Case No.	Dorsal		Middle		Ventral		Medial	
		L.	R.	L.	R.	L.	R.	L.	R.
1942	4	+	+	+	+			+	+
	7			+					
	8								
	10			+	+	+	+		
	26		+	+	+				
	27			+	+				
1943	(1)	+	+	+	+	+	+	+	+
	(2)	+	+	+	+	+			
	3	+		+	+				
	5	+	+			+	+	+	+
	9			+	+				
	12	+	+	+	+	+		+	+
	18	+	+	+		+	+	+	
1944	11			+	+	+	+	+	
	14			+	+				
	20	+		+	+			+	
	21			+	+				
1945	13	+	+	+	+				
	(15)			+	+		+		
	16	+		+	+	+	+		
	19			+	+				
1946	(17)		+	+	+			+	+
	22	+		+	+			+	
	(23)	+	+		+	+	+	+	+
	(24)	+	+	+		+		+	+
	(25)			+	+				
	(28)	+	+	+	+	+	+	+	+

(Case No. 6 was a lobectomy.)

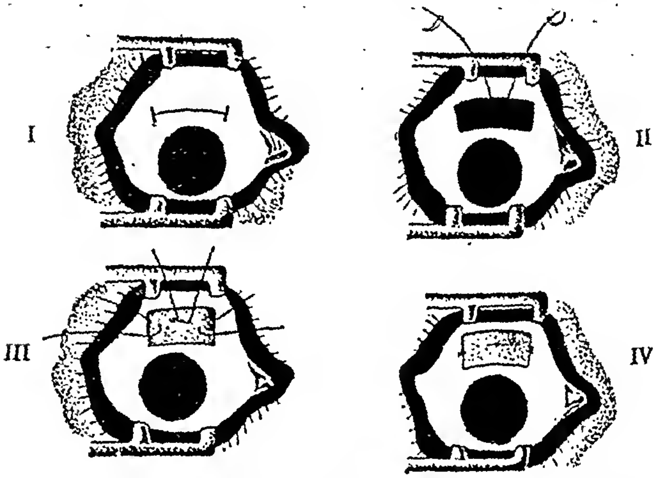


Diagram I.—Incision of the conjunctiva bulbi. Diagram II.—The flap of the conjunctiva bulbi is excised and a stitch is passed. Diagram III.—The flap of the mucosa of the lip now covers the wound and stitches are passed. Diagram IV.—Operation completed.
(*After* Prof. V. P. Filatoff: "Optical Transplant of the Cornea", Odessa, 1945.)

Result of operation.—(1) L.V. Before operation: V.A.—Counting fingers at 2 metres; (2) L.V. After operation: Counting fingers at 4 metres.

Retinal Hæmorrhage with Mitral Incompetence.—NOAH PINES, M.B.

This case of advanced mitral incompetence, which was of many years standing, was in a man aged 34.

October 23, 1946: He helped to move a heavy object, and on the following day developed a troublesome cough. Two days later a large venous hæmorrhage appeared in the left eye at the 6 o'clock position. B.P. was: right arm $\frac{100/90}{60}$ mean 80, oscil. 7; left arm: $\frac{100/90}{60}$ mean 60, oscil. 4.

November 1, 1946: The hæmorrhage in the left eye had completely gone, without leaving any trace, but in the right eye there appeared a fresh striate, rather large hæmorrhage covering the secondary branch of an artery at the 2 o'clock position, already with a white spot in it.

Dr. Pines gave an illustrated account of the instrumental methods used in examination: (1) Bailliart's dynamometer for measuring the retinal arterial pressure; (2) Pachon's oscillometer for measuring the brachial arterial pressure and oscillometry.

REFERENCES

BAILLIART, P. (1923) La Circulation rétinienne. Paris.
PACHON, V., and FABRE, R. (1934) Clinical Investigation of Cardiovascular Function. London.

The President, speaking of the cases in which Denig's operation had been performed, said that this operation was very successful. He well remembered a case in which he was concerned with another member of the Section many years ago in which the result was very gratifying.

Section of Psychiatry

President—Professor AUBREY LEWIS, M.D.

[*December* 10, 1946]

DISCUSSION: LEUCOTOMY AS AN INSTRUMENT OF RESEARCH

Dr. A. Meyer and Dr. T. McLardy: *Neuropathological studies* [*Abridged*].—Prefrontal leucotomy, in pursuing its therapeutic purpose, is furnishing us with a human experiment on the function of the frontal lobes on a scale comparable in its potentialities perhaps only with the first world war's head injuries which contributed such a wealth of new knowledge through the work of Head, Holmes, Goldstein and others.

The neuropathological (and neuro-anatomical) is of course only one among the many aspects of this experiment. Valuable opportunities of research are offered in many other fields including neurology, psychology and pharmacology. The neuro-pathological side of the problem is of some special importance because most, if not all, of the clinical research work would be largely invalid without ultimate pathological control.

The importance of pathological control is illustrated by the following table which shows both hemispheres in all our cases at present numbering 27, analysed in terms of the segments involved in the cut. It demonstrates clearly the variability of the lesions and that in only a few cases was the general aim attained of a bilateral lesion

		SEGMENT CUT							
	Case	Dorsal		Middle		Ventral		Medial	
Year of opn.	No.	L.	R.	L.	R.	L.	R.	L.	R.
1942	4	+	+	+	+			+	+
	7			+					
	8								
	10			+	+	+	+		
	26		+	+	+				
	27			+	+				
1943	(1)	+	+	+	+	+	+	+	+
	(2)	+	+	+	+	+			
	3	+		+	+				
	5	+	+			+	+	+	+
	9			+	+				
	12	+	+	+	+	+		+	+
	18	+	+	+		+	+	+	
1944	11			+	+	+	+	+	
	14			+	+				
	20	+		+	+			+	
	21			+	+				
1945	13	+	+	+	+				
	(15)			+	+		+		
	16	+		+	+	+	+		
	19			+	+				
1946	(17)		+	+	+			+	+
	22	+		+	+			+	
	(23)	+	+		+	+	+	+	+
	(24)	+	+	+		+		+	+
	(25)			+	+				
	(28)	+	+	+	+	+	+	+	+

(Case No. 6 was a lobectomy.)

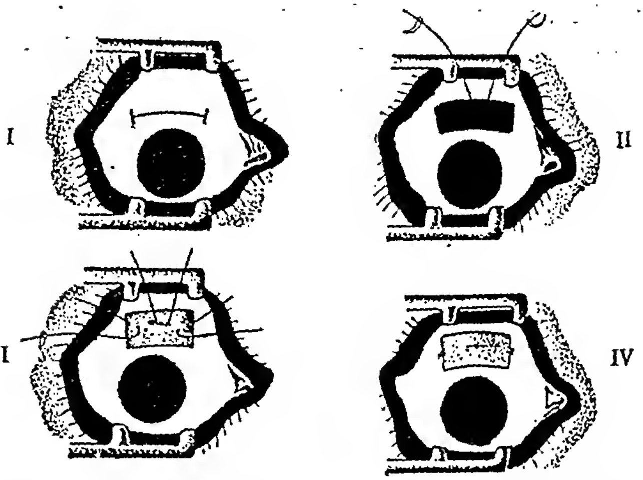


Diagram I.—Incision of the conjunctiva bulbi. Diagram II.—The flap of the conjunctiva bulbi is excised and a stitch is passed. Diagram III.—The flap of the mucosa of the lip now covers the wound and stitches are passed. Diagram IV.—Operation completed.
(*After* Prof. V. P. Filatoff: "Optical Transplant of the Cornea", Odessa, 1945.)

Result of operation.—(1) L.V. Before operation: V.A.—Counting fingers at 2 metres; (2) L.V. After operation: Counting fingers at 4 metres.

Retinal Hæmorrhage with Mitral Incompetence.—Noah Pines, M.B.

This case of advanced mitral incompetence, which was of many years standing, was in a man aged 34.

October 23, 1946: He helped to move a heavy object, and on the following day developed a troublesome cough. Two days later a large venous hæmorrhage appeared in the left eye at the 6 o'clock position. B.P. was: right arm $\frac{100/00}{60}$ mean 80, oscil. 7; left arm: $\frac{100/00}{50}$ mean 60, oscil. 4.

November 1, 1946: The hæmorrhage in the left eye had completely gone, without leaving any trace, but in the right eye there appeared a fresh striate, rather large hæmorrhage covering the secondary branch of an artery at the 2 o'clock position, already with a white spot in it.

Dr. Pines gave an illustrated account of the instrumental methods used in examination: (1) Bailliart's dynamometer for measuring the retinal arterial pressure; (2) Pachon's oscillometer for measuring the brachial arterial pressure and oscillometry.

REFERENCES

Bailliart, P. (1923) La Circulation rétinienne. Paris.
Pachon, V., and Fabre, R. (1934) Clinical Investigation of Cardiovascular Function. London.

The President, speaking of the cases in which Denig's operation had been performed, said that this operation was very successful. He well remembered a case in which he was concerned with another member of the Section many years ago in which the result was very gratifying.

significantly larger in man than in the chimpanzee, in striking contrast to the temporal and parietal lobes which steadily enlarge from monkeys to man. This is supported by the oscillographic work by Kennard and McCulloch (1944). As a corollary to this it is interesting to remember that it is the theta rhythm, now believed to be the normal E.E.G. rhythm of the human temporo-parietal region, which is abnormal in conditions of immaturity, behaviour problems in children and aggressive psychopathy (Hill, 1945) . Furthermore, the temporal lobe possesses the distinction of containing the only cerebral cortex devoid of thalamic projection (Walker, 1938). While these findings do not disprove the preoccupation of the frontal lobes with emotional and personality integration, they cast some doubt on the validity of using gross phylogenetic data in contending that the frontal lobes are man's greatest developmental achievement and therefore likely to be particularly concerned in his highest mental activities.

Serious criticism of the frontal lobe localization has come also from the clinical side. A specific personality change caused by lesions in the frontal lobes has never been generally accepted in this country. Walshe (1931) has recognized a frontal lobe syndrome, but one recalls an earlier joint meeting of this and the Neurological Section when only Gordon Holmes (1931) acknowledged the concept of personality changes due to frontal lobe tumours, whilst Kinnier Wilson, Mapother, Golla, Symonds and Worster-Drought more or less definitely rejected it.

The issue has been quite recently taken up by Hebb (1945) whose critical review on "Man's Frontal Lobes" seems to have aroused lively interest in this country. We agree with several of his critical points, and in particular that in all cases of bilateral pathological involvement or surgical removal of the frontal lobes there is the possibility that the pathological process itself may be more responsible for the mental changes than the loss of frontal lobe tissue. We disagree, however, with his evaluation of Hebb and Penfield's (1940) personal case as an instance of minimal, or even absent, deficit syndrome after bilateral lobectomy. The previous personality of an adolescent, even when known, cannot be taken as a reliable control guide to what his personality would have become after full uninterrupted maturation.

Hebb explicitly rejects the evidence from prefrontal leucotomy because of the uncertainty of the extent of the anatomical defect caused by the surgical lesions and the possibility of undetected pathological complications. He did not perceive that, provided it were possible to obtain a sufficient number of leucotomized brains from patients dying from intercurrent causes, and that clinical and psychological examinations before and after the operation were adequate, then all the conditions which he demands would be fulfilled, although of course it should not be forgotten that leucotomy is not identical with lobectomy. Our material is as yet too limited and too unevenly investigated clinically, as well as pathologically, to fulfil these conditions; but even a provisional analysis gives some concrete idea of the potentialities of such an investigation, as the following brief survey may indicate.

In 6 out of the 19 patients who survived long enough for adequate clinical observation (from seven weeks to almost four years) symptoms of a frontal lobe deficit syndrome, such as euphoria, facetiousness, apathy, lack of initiative or overactivity, were recorded. In these cases we found little evidence of pathological changes different from those in the other cases, which might have caused the syndrome. In others of the 19 cases one cannot exclude that minor degrees of a similar personality change may have been overlooked for almost all our cases, though some showed improvement, remained institutionalized, and according to Ström-Olsen (1946) the personality changes often do not manifest themselves before the patient has returned to his normal environment. The variation in the location

through the whole of the white matter. (The case numbers of the 8 who died within seven weeks of operation are bracketed.) The variability in the plane of the cut which was demonstrated in a previous paper by Meyer and Beck (1945) was also apparent in this extended series of cases.

Each case, and often each hemisphere, presents as it were a separate human experiment. As most of our knowledge of the structural as well as functional organization of the frontal lobe and its connexions is based upon experimental work on animals, and human brains with concise lesions are rare, there is no need to emphasize the importance of investigating leucotomized brains from a comparative anatomical point of view. We have paid particular attention to the organization of the thalamo-frontal projections, especially of the dorsomedial nucleus; the fronto-pontine tract and, in particular, that prefronto-pontine part of the tract known as Arnold's bundle, which has not yet been investigated in the human brain; and the so-called long association tracts, whose anatomy and function are still shrouded in considerable obscurity. A detailed account of the anatomical findings in 10 fully investigated cases (extending the initial observations of Meyer and Beck, 1945) will be published shortly in *Brain* jointly with Mrs. Beck, to whom we are greatly indebted for much help in the preparation of this paper. We also at this point would like to express our gratitude to the many clinicians who have supplied us with the 27 brains and case-histories.

Turning to the clinico-pathological aspects of our material, the most arresting problem is that of personality changes which may follow lesions in the prefrontal region and which may throw light upon the wider problem of frontal lobe function. We shall confine our attention essentially to the question of the reality of the personality changes, and their possible substrate, and not concern ourselves with the various general theories of frontal lobe function. There is no need to define the term frontal lobe deficit syndrome after the many human and experimental contributions made on this subject, and the exhaustive reviews of the whole problem in the important monographs of Rylander (1939) and of Freeman and Watts (1942).

Of attempts at localization of mental activity, the most detailed and probably the most "atomistic" is that of Kleist (1934) who ascribes a special function to almost every Brodmann area: e.g. initiative to area 9; motor skill to area 10; constructive thinking to the middle frontal region (area 46); sentiment to the lateral orbital region (area 47); and personal and social ego to area 11. Kleist (1937) also stressed the relation of the prefrontal region to the hypothalamic-thalamic complex and the cingulate gyrus, a combination of centres which in modified form was presented by Papez (1937) as a cerebral mechanism of emotion and emotional expression. Yet another variant of Kleist's scheme is Spatz's (1937) concept of the "basal cortex", comprising the ventral parts of the frontal and temporal lobes, which he suggests may be concerned especially with emotional and personality integration. This last conception of the basal cortex as an entity has, from a functional organization point of view, recently been strengthened by the oscillographic work of McCulloch (1944) and his associates.

Criticisms of these concepts of frontal lobe localization have been made from several angles. The whole principle of localization of mental symptoms in the brain has been severely criticized by Lashley (1937), Masserman (1943), Golla (1946) and others. These criticisms are justified, we consider, only against the crudities of mechanistic localization. The concepts of localized and holistic function, as has been pointed out by Sherrington (1940), are not mutually exclusive: on the contrary, they are complementary.

There is also a possible criticism from the comparative anatomical angle. Recent work by von Bonin (1941) has shown that the volume of the frontal lobe is not

significantly larger in man than in the chimpanzee, in striking contrast to the temporal and parietal lobes which steadily enlarge from monkeys to man. This is supported by the oscillographic work by Kennard and McCulloch (1944). As a corollary to this it is interesting to remember that it is the theta rhythm, now believed to be the normal E.E.G. rhythm of the human temporo-parietal region, which is abnormal in conditions of immaturity, behaviour problems in children and aggressive psychopathy (Hill, 1945). Furthermore, the temporal lobe possesses the distinction of containing the only cerebral cortex devoid of thalamic projection (Walker, 1938). While these findings do not disprove the preoccupation of the frontal lobes with emotional and personality integration, they cast some doubt on the validity of using gross phylogenetic data in contending that the frontal lobes are man's greatest developmental achievement and therefore likely to be particularly concerned in his highest mental activities.

Serious criticism of the frontal lobe localization has come also from the clinical side. A specific personality change caused by lesions in the frontal lobes has never been generally accepted in this country. Walshe (1931) has recognized a frontal lobe syndrome, but one recalls an earlier joint meeting of this and the Neurological Section when only Gordon Holmes (1931) acknowledged the concept of personality changes due to frontal lobe tumours, whilst Kinnier Wilson, Mapother, Golla, Symonds and Worster-Drought more or less definitely rejected it.

The issue has been quite recently taken up by Hebb (1945) whose critical review on "Man's Frontal Lobes" seems to have aroused lively interest in this country. We agree with several of his critical points, and in particular that in all cases of bilateral pathological involvement or surgical removal of the frontal lobes there is the possibility that the pathological process itself may be more responsible for the mental changes than the loss of frontal lobe tissue. We disagree, however, with his evaluation of Hebb and Penfield's (1940) personal case as an instance of minimal, or even absent, deficit syndrome after bilateral lobectomy. The previous personality of an adolescent, even when known, cannot be taken as a reliable control guide to what his personality would have become after full uninterrupted maturation.

Hebb explicitly rejects the evidence from prefrontal leucotomy because of the uncertainty of the extent of the anatomical defect caused by the surgical lesions and the possibility of undetected pathological complications. He did not perceive that, provided it were possible to obtain a sufficient number of leucotomized brains from patients dying from intercurrent causes, and that clinical and psychological examinations before and after the operation were adequate, then all the conditions which he demands would be fulfilled, although of course it should not be forgotten that leucotomy is not identical with lobectomy. Our material is as yet too limited and too unevenly investigated clinically, as well as pathologically, to fulfil these conditions; but even a provisional analysis gives some concrete idea of the potentialities of such an investigation, as the following brief survey may indicate.

In 6 out of the 19 patients who survived long enough for adequate clinical observation (from seven weeks to almost four years) symptoms of a frontal lobe deficit syndrome, such as euphoria, facetiousness, apathy, lack of initiative or overactivity, were recorded. In these cases we found little evidence of pathological changes different from those in the other cases, which might have caused the syndrome. In others of the 19 cases one cannot exclude that minor degrees of a similar personality change may have been overlooked for almost all our cases, though some showed improvement, remained institutionalized, and according to Ström-Olsen (1946) the personality changes often do not manifest themselves before the patient has returned to his normal environment. The variation in the location

through the whole of the white matter. (The case numbers of the 8 who died within seven weeks of operation are bracketed.) The variability in the plane of the cut which was demonstrated in a previous paper by Meyer and Beck (1945) was also apparent in this extended series of cases.

Each case, and often each hemisphere, presents as it were a separate human experiment. As most of our knowledge of the structural as well as functional organization of the frontal lobe and its connexions is based upon experimental work on animals, and human brains with concise lesions are rare, there is no need to emphasize the importance of investigating leucotomized brains from a comparative anatomical point of view. We have paid particular attention to the organization of the thalamo-frontal projections, especially of the dorsomedial nucleus; the fronto-pontine tract and, in particular, that prefronto-pontine part of the tract known as Arnold's bundle, which has not yet been investigated in the human brain; and the so-called long association tracts, whose anatomy and function are still shrouded in considerable obscurity. A detailed account of the anatomical findings in 10 fully investigated cases (extending the initial observations of Meyer and Beck, 1945) will be published shortly in *Brain* jointly with Mrs. Beck, to whom we are greatly indebted for much help in the preparation of this paper. We also at this point would like to express our gratitude to the many clinicians who have supplied us with the 27 brains and case-histories.

Turning to the clinico-pathological aspects of our material, the most arresting problem is that of personality changes which may follow lesions in the prefrontal region and which may throw light upon the wider problem of frontal lobe function. We shall confine our attention essentially to the question of the reality of the personality changes, and their possible substrate, and not concern ourselves with the various general theories of frontal lobe function. There is no need to define the term frontal lobe deficit syndrome after the many human and experimental contributions made on this subject, and the exhaustive reviews of the whole problem in the important monographs of Rylander (1939) and of Freeman and Watts (1942).

Of attempts at localization of mental activity, the most detailed and probably the most "atomistic" is that of Kleist (1934) who ascribes a special function to almost every Brodmann area: e.g. initiative to area 9; motor skill to area 10; constructive thinking to the middle frontal region (area 46); sentiment to the lateral orbital region (area 47); and personal and social ego to area 11. Kleist (1937) also stressed the relation of the prefrontal region to the hypothalamic-thalamic complex and the cingulate gyrus, a combination of centres which in modified form was presented by Papez (1937) as a cerebral mechanism of emotion and emotional expression. Yet another variant of Kleist's scheme is Spatz's (1937) concept of the "basal cortex", comprising the ventral parts of the frontal and temporal lobes, which he suggests may be concerned especially with emotional and personality integration. This last conception of the basal cortex as an entity has, from a functional organization point of view, recently been strengthened by the oscillographic work of McCulloch (1944) and his associates.

Criticisms of these concepts of frontal lobe localization have been made from several angles. The whole principle of localization of mental symptoms in the brain has been severely criticized by Lashley (1937), Masserman (1943), Golla (1946) and others. These criticisms are justified, we consider, only against the crudities of mechanistic localization. The concepts of localized and holistic function, as has been pointed out by Sherrington (1940), are not mutually exclusive: on the contrary, they are complementary.

There is also a possible criticism from the comparative anatomical angle. Recent work by von Bonin (1941) has shown that the volume of the frontal lobe is not

significantly larger in man than in the chimpanzee, in striking contrast to the temporal and parietal lobes which steadily enlarge from monkeys to man. This is supported by the oscillographic work by Kennard and McCulloch (1944). As a corollary to this it is interesting to remember that it is the theta rhythm, now believed to be the normal E.E.G. rhythm of the human temporo-parietal region, which is abnormal in conditions of immaturity, behaviour problems in children and aggressive psychopathy (Hill, 1945) . Furthermore, the temporal lobe possesses the distinction of containing the only cerebral cortex devoid of thalamic projection (Walker, 1938). While these findings do not disprove the preoccupation of the frontal lobes with emotional and personality integration, they cast some doubt on the validity of using gross phylogenetic data in contending that the frontal lobes are man's greatest developmental achievement and therefore likely to be particularly concerned in his highest mental activities.

Serious criticism of the frontal lobe localization has come also from the clinical side. A specific personality change caused by lesions in the frontal lobes has never been generally accepted in this country. Walshe (1931) has recognized a frontal lobe syndrome, but one recalls an earlier joint meeting of this and the Neurological Section when only Gordon Holmes (1931) acknowledged the concept of personality changes due to frontal lobe tumours, whilst Kinnier Wilson, Mapother, Golla, Symonds and Worster-Drought more or less definitely rejected it.

The issue has been quite recently taken up by Hebb (1945) whose critical review on "Man's Frontal Lobes" seems to have aroused lively interest in this country. We agree with several of his critical points, and in particular that in all cases of bilateral pathological involvement or surgical removal of the frontal lobes there is the possibility that the pathological process itself may be more responsible for the mental changes than the loss of frontal lobe tissue. We disagree, however, with his evaluation of Hebb and Penfield's (1940) personal case as an instance of minimal, or even absent, deficit syndrome after bilateral lobectomy. The previous personality of an adolescent, even when known, cannot be taken as a reliable control guide to what his personality would have become after full uninterrupted maturation.

Hebb explicitly rejects the evidence from prefrontal leucotomy because of the uncertainty of the extent of the anatomical defect caused by the surgical lesions and the possibility of undetected pathological complications. He did not perceive that, provided it were possible to obtain a sufficient number of leucotomized brains from patients dying from intercurrent causes, and that clinical and psychological examinations before and after the operation were adequate, then all the conditions which he demands would be fulfilled, although of course it should not be forgotten that leucotomy is not identical with lobectomy. Our material is as yet too limited and too unevenly investigated clinically, as well as pathologically, to fulfil these conditions; but even a provisional analysis gives some concrete idea of the potentialities of such an investigation, as the following brief survey may indicate.

In 6 out of the 19 patients who survived long enough for adequate clinical observation (from seven weeks to almost four years) symptoms of a frontal lobe deficit syndrome, such as euphoria, facetiousness, apathy, lack of initiative or overactivity, were recorded. In these cases we found little evidence of pathological changes different from those in the other cases, which might have caused the syndrome. In others of the 19 cases one cannot exclude that minor degrees of a similar personality change may have been overlooked for almost all our cases, though some showed improvement, remained institutionalized, and according to Ström-Olsen (1946) the personality changes often do not manifest themselves before the patient has returned to his normal environment. The variation in the location

through the whole of the white matter. (The case numbers of the 8 who died within seven weeks of operation are bracketed.) The variability in the plane of the cut which was demonstrated in a previous paper by Meyer and Beck (1945) was also apparent in this extended series of cases.

Each case, and often each hemisphere, presents as it were a separate human experiment. As most of our knowledge of the structural as well as functional organization of the frontal lobe and its connexions is based upon experimental work on animals, and human brains with concise lesions are rare, there is no need to emphasize the importance of investigating leucotomized brains from a comparative anatomical point of view. We have paid particular attention to the organization of the thalamo-frontal projections, especially of the dorsomedial nucleus; the fronto-pontine tract and, in particular, that prefronto-pontine part of the tract known as Arnold's bundle, which has not yet been investigated in the human brain; and the so-called long association tracts, whose anatomy and function are still shrouded in considerable obscurity. A detailed account of the anatomical findings in 10 fully investigated cases (extending the initial observations of Meyer and Beck, 1945) will be published shortly in *Brain* jointly with Mrs. Beck, to whom we are greatly indebted for much help in the preparation of this paper. We also at this point would like to express our gratitude to the many clinicians who have supplied us with the 27 brains and case-histories.

Turning to the clinico-pathological aspects of our material, the most arresting problem is that of personality changes which may follow lesions in the prefrontal region and which may throw light upon the wider problem of frontal lobe function. We shall confine our attention essentially to the question of the reality of the personality changes, and their possible substrate, and not concern ourselves with the various general theories of frontal lobe function. There is no need to define the term frontal lobe deficit syndrome after the many human and experimental contributions made on this subject, and the exhaustive reviews of the whole problem in the important monographs of Rylander (1939) and of Freeman and Watts (1942).

Of attempts at localization of mental activity, the most detailed and probably the most "atomistic" is that of Kleist (1934) who ascribes a special function to almost every Brodmann area: e.g. initiative to area 9; motor skill to area 10; constructive thinking to the middle frontal region (area 46); sentiment to the lateral orbital region (area 47); and personal and social ego to area 11. Kleist (1937) also stressed the relation of the prefrontal region to the hypothalamic-thalamic complex and the cingulate gyrus, a combination of centres which in modified form was presented by Papez (1937) as a cerebral mechanism of emotion and emotional expression. Yet another variant of Kleist's scheme is Spatz's (1937) concept of the "basal cortex", comprising the ventral parts of the frontal and temporal lobes, which he suggests may be concerned especially with emotional and personality integration. This last conception of the basal cortex as an entity has, from a functional organization point of view, recently been strengthened by the oscillographic work of McCulloch (1944) and his associates.

Criticisms of these concepts of frontal lobe localization have been made from several angles. The whole principle of localization of mental symptoms in the brain has been severely criticized by Lashley (1937), Masserman (1943), Golla (1946) and others. These criticisms are justified, we consider, only against the crudities of mechanistic localization. The concepts of localized and holistic function, as has been pointed out by Sherrington (1940), are not mutually exclusive: on the contrary, they are complementary.

There is also a possible criticism from the comparative anatomical angle. Recent work by von Bonin (1941) has shown that the volume of the frontal lobe is not

REFERENCES

Bonin, G. von (1941) *J. Comp. Neurol.*, 75, 287.
Dax, E. C., and Radley-Smith, E. J. (1946) *Proc. R. Soc. Med.*, 39, 448.
Freeman, W., and Watts, J. W. (1942) Psychosurgery. Springfield.
—— (1944) *Ann. Rev. Physiol.*, 6, 517.
Golla, F. L. (1946) *Proc. R. Soc. Med.*, 39, 443.
Hebb, D. O. (1945) *Arch. Neurol. Psychiat., Chicago*, 54, 10.
—— and Penfield, W. (1940) *Arch. Neurol. Psychiat., Chicago*, 44, 421.
Hill, D. (1945) *J. ment. Sci.*, 91, 281.
Holmes, G. *et al.* (1931) *Proc. R. Soc. Med.*, 24, 997.
Kennard, M. A. (1935) *Arch. Neurol. Psychiat., Chicago*, 33, 537.
Kennard, M. A., and McCulloch, W. S. (1944) *J. Neurophysiol.*, 7, 37.
Kleist, K. (1934) Handbuch der ärztlichen Erfahrungen im Weltkriege, Leipzig, 4.
—— (1937) *Z. ges. Neurol. Psychiat.*, 158, 159.
Knight, G. C. (1943) *J. ment. Sci.*, 89, 174.
Lashley, K. B. (1937) *Arch. Neurol. Psychiat., Chicago*, 38, 371.
Masserman, J. H. (1943) Behaviour and Neurosis. Chicago.
McCulloch, W. S. (1944) *Physiol. Rev.*, 24, 390.
Mettler, F. A. (1945) *J. Neuropath.*, 4, 99.
Meyer, A., and Beck, E. (1945) *J. ment. Sci.*, 91. 411.
Papez, J. W. (1937) *Arch. Neurol. Psychiat., Chicago*, 38, 725.
—— (1940) *Trans. Amer. Neurol. Ass.*, 66, 128.
Rylander, G. (1939) *Acta Psychiat. Neurol.*, Suppl. 20.
Sherrington, C. (1940) Man on his Nature. Camb. Univ. Press.
Smith, W. K. (1945) *J. Neurophysiol.*, 8, 241.
Spatz, H. (1937) *Z. ges. Neurol. Psychiat.*, 158, 208.
Ström-Olsen, R. (1946) *Proc. R. Soc. Med.*, 39, 451.
Walker, A. E. (1938) The Primate Thalamus. Chicago.
Walshe, F. M. R. (1931) *Quart. J. Med.*, 24, 587.
Ziegler, L. H., and Osgood, C. W. (1945) *Arch. Neurol. Psychiat., Chicago*, 53, 262.

Dr. G. D. Greville and Dr. S. L. Last: *Leucotomy as an instrument of research. Electroencephalographic studies* [*Abridged*].—The material consisted of 35 cases, involving various psychiatric disorders. The operations were all performed by Mr. G. C. Knight, who employed in most of them Crombie's technique combined with that of Freeman and Watts. The E.E.G. was recorded whenever possible before leucotomy and again one day, ten days, three weeks, six weeks, three months, six months and one year after the operation: but on several occasions the state of the patient did not permit the examination, and on others the record had to be discarded on account of interfering artefacts due to the patient's restlessness and lack of co-operation.

Alpha activity (8 to 13 c/s).—Table I shows that the voltage of the alpha rhythm tends to increase after the operation. In some cases the voltage increases, in others it decreases and in a certain proportion it remains the same, but at one day after the operation more show an increase than a decrease, and this becomes more pronounced after three weeks. By "amount" of alpha activity (Table I) we mean the relative length of record occupied by this rhythm, e.g. whether it occurs continuously, or for half the time or only in short runs. The amount seems to increase after the operation, the tendency being most noticeable after ten days. The records of three cases studied by Davis (1941) show an increase in alpha voltage after leucotomy, and Cohn (1945) has remarked on an enhancement of alpha activity after the operation in Freeman and Watts's patients.

Table I.—Alpha Activity.
Number of records in which the voltage (or amount) was greater than, equal to, or less than that before the operation.

		Time after operation						
		1 day	10 days	3 weeks	6 weeks	3 months	6 months	1 year
Voltage	Greater	10	10	19	12	6	11	4
	Equal	3	6	4	3	2	1	0
	Less	6	6	0	2	2	1	1
Amount	Greater	8	10	10	7	4	7	1
	Equal	3	8	6	9	4	2	2
	Less	5	1	3	0	2	4	1

and extent of the cut may well account for some of the conflicting reports in the literature on the frequency, severity and variety of the personality change. In several of our cases indeed the damage to the prefrontal region was negligible.

A study of cases having wide variation of the position of the lesion in the prefrontal region also provides an opportunity of testing, for instance, Kleist's map (1934) of frontal lobe function, and kindred suggestions recently made by Dax and Radley-Smith (1946) for specific cuts: aggression to be alleviated by a dorsal, paranoid symptoms by a middle cut, and depression and tension by a cut nearer to the orbital region. In our material so far there may be a positive trend of correlation between improvement of depressive symptoms and orbital region involvement; but in the case exhibiting the severest degree of post-operative euphoria the orbital region was intact on both sides. For the other two types of case we have so far found no evidence of a positive correlation of improvement with the suggested cut. Further and more detailed observations are necessary, taking careful account as well of non-anatomical variables, such as previous personality and life-history.

Freeman and Watts (1944) observed during the operation that a previously responsive patient will drift into confusion when the medial segments of the prefrontal region are cut bilaterally. It is, therefore, interesting that the only 3 cases (among these 19) in which a post-operative confusion (of several days' duration) was noted were also the only ones with bilateral involvement of this medial segment (mainly of the Brodmann areas 32 and 24). Freeman and Watts's contention that this confusion is an essential factor in the mechanism of recovery is not borne out by these 3 cases or our material generally. It is uncertain what this symptom means in terms of physiology. Freeman and Watts (1944) favour involvement of the cingulate fasciculus rather than the cutting of callosal fibres as the operative factor. It will be remembered too that area 24 has been considered to be concerned with emotional expression (Papez, 1940; Smith, 1945) and that McCulloch (1944) regards area 32 as part of the "cingular belt" in which impulses coming from cortical suppressor bands are collected and where, thus, important cerebral activity appears to be concentrated.

In 2 of the cases in which the striatal region was involved in the cut severe restlessness and, in one case, rhythmic movements of the head, were mentioned in the case-notes. This might be of some significance in view of Mettler's (1945) similar observation in monkeys.

In 2 other patients developing after the operation marked vasomotor and trophic disturbances in the extremities area 6 was bilaterally involved. This recalls Kennard's (1935) earlier findings after ablation of the premotor area in monkeys, Knight's (1943) report of trophic disturbances following an unduly caudal leucotomy cut, and Ziegler and Osgood's (1945) report of such disturbances which they thought due to damage to areas 4, 6 and 8.

These few examples may suffice to demonstrate the importance of leucotomy as an instrument of research in neuropathological spheres. There are many other clinico-pathological correlations for which we are accumulating data, for instance, concerning post-operative epilepsy, speech defect, incontinence and disturbance of eye movements. They demonstrate also, we hope, the urgent need of a co-ordinated effort which must include on the one hand the fullest and most standardized clinical investigation in all directions before and after operation, and, on the other hand, effective arrangements for procuring the brain of patients dying from intercurrent illness. This will be a laborious research, but it should eventually furnish a decisive answer to many of our problems.

Theta activity (4 to 7 c/s).—This was widespread, with a tendency to frontal regions and no clear localization; the most common frequencies were 5 and 6 c/s. It occurred in a higher percentage of cases than delta activity and this percentage remained more constant with time. Table III shows that after the initial rise at ten days the frequency of occurrence of theta activity stayed constant at about 60 per cent., while that of delta dropped between three weeks and three months. This is scarcely in agreement with the statement of Cohn (1945) that theta activity gradually replaces delta in these cases. It should be pointed out, however, that while theta activity continued to appear in the later records, the amount in each record tended to diminish.

Following an operation which frequently either increases or decreases the aggressiveness of the patient it is natural to consider whether there is a connexion between aggressiveness and theta activity, since the latter is of frequent occurrence in aggressive psychopaths, as was first shown by Hill and Watterson (1942). We cannot, however, say that theta waves appeared particularly often when patients became aggressive, or rarely when they were apathetic or dull. This is scarcely surprising, however, since theta activity is by no means restricted to aggressive psychopathy, but occurs with subcortical tumours, epilepsy, &c., as well as in childhood and adolescence.

Discussion: *Causation of the delta activity.*—Delta activity is customarily regarded as arising from grey matter which has been damaged, as in head injuries or by a tumour, or is functioning at a reduced level, as in sleep, coma, hypoglycæmia or anoxia; that is, cortical cells the function or metabolism of which have been affected tend to discharge synchronously at a low frequency. In our cases we have seen that after the first few days, when the initial widespread disturbance has abated, the delta waves arise in general from the part of the cortex in front of the cut. It is possible that the delta activity then comes from those cell groups which have suffered direct damage from the operation, or more particularly through the cutting of their axons. On the other hand Meyer and Beck (1945) have shown that only comparatively few cells in the prefrontal cortex suffer permanent damage after leucotomy. We therefore suggest that it is the functional isolation of the prefrontal cortex from the rest of the brain which causes large groups of cells in the former to discharge synchronously. Bremer (1935) found that high-voltage activity in bursts results from deafferentation of the cortex in the *cerveau isolé* preparation of the cat. Kennard and Nims (1942), in experiments on monkeys, found an absence of abnormal waves when cortex only was removed, whereas slow activity appeared when the basal ganglia were partially destroyed. Here again, therefore, slow activity appeared when the cortex was deprived of the influence of some of the subcortical structures with which it is normally connected. The kind of problem we have been discussing may come nearer to solution when the brains of cases investigated with the E.E.G. can be examined histologically.

We should like to thank Dr. R. Ström-Olsen for his help and advice, and our collaborators, Miss J. E. H. Munson, Mr. P. St.John-Loe and Mr. D. Lee, for their patient work.

REFERENCES

BREMER, F. (1935) *C. R. Soc. Biol. Paris*, 118, 1235.
COHN, R. (1945) *Arch. Neurol. Psychiat. Chicago*, 53, 274.
DAVIS, P. A. (1941) *Psychosom. Med.*, 3, 38.
HILL, D., and WATTERSON, D. (1942) *J. Neurol. Psychiat.*, 5 (N.S.), 47.
KENNARD, M. A., and NIMS, L. F. (1942) *J. Neurophysiol.*, 5, 335.
MEYER, A., and BECK, E. (1945) *J. ment. Sci.*, 91. 411.

Dr. F. Reitman: Leucotomy as an instrument of research has been discussed from the neuropathological and electroencephalographic aspects. Physiological research is being conducted at Netherne Hospital in connexion with this subject. Experi-

TABLE II.—FAST ACTIVITY.

Number of records at different times with high, medium and low voltage fast activity, and with large, medium and small amounts of fast activity.

		Before operation	Time after operation						
			1 day	10 days	3 weeks	6 weeks	3 months	6 months	1 year
Voltage	High	6	3	2	3	3	2	2	0
	Medium	5	4	8	8	8	6	7	3
	Low	6	9	10	8	7	3	5	1
Amount	Large	10	8	4	6	7	2	5	2
	Medium	3	1	3	1	1	3	3	2
	Small	1	2	4	5	2	1	3	0

Fast activity (frequencies greater than 13 c/s).—The voltage of the fast activity tends to diminish after the operation, and there is some indication that the amount tends to decrease also (Table II).

The increase in alpha activity and decrease in fast activity may point to a greater ability to relax following the operation, and possibly the decrease in emotional tension displayed by many leucotomized patients is reflected in this alteration in the record. On the other hand, ability to relax may increase as the patient becomes used to the examination; for various reasons, however, we do not consider that this provides the full explanation.

Delta activity (frequencies less than 4 c/s).—Considerable technical difficulties were encountered here as the potentials arising from eye movements may be confused with frontal delta waves, and special methods had to be employed to distinguish eye movement artefacts from cortical potentials. Delta activity is fairly common after leucotomy, more than half our cases showing it at some time. If it is going to appear it usually appears by one day after the operation, certainly by ten days; thereafter it is seen in fewer cases, and in smaller amounts in individual records. At first delta activity may appear all over the cortex, but it soon becomes predominant in the frontal areas. At this time it may show some extension to central areas, but this gradually disappears, until after three weeks there is little delta activity which does not come from the front.

When an attempt at accurate location was made it was found, with dipolar recording, that the delta activity originated in front of the cut. Indeed, the indication was that it arose in the prefrontal areas. We are in agreement with Cohn (1945) who, with a monopolar derivation, found more delta activity the further forward he placed his electrodes. The delta waves were often strictly synchronous in the two hemispheres; and another feature was that whereas at first the waves appeared at random, after ten days the rhythm became more paroxysmal in nature.

One of the problems of delta activity is its correlation with age. Delta rhythms occur normally in children and disappear with increasing age. Abnormal rhythms are also dependent on age, since epilepsy and head injury show a diminishing tendency to produce slow activity in increasing age-groups. In our cases, however, there appears to be no correlation between delta activity and age. About 57 per cent. of the total cases developed delta activity; it was observed in 4 out of the 9 cases under 30 years, and in 16 out of the 26 over 30 years of age. It thus occurred with roughly the same frequency in the two age-groups; and a similar result is obtained if one considers patients above and below 35 years of age. There is some indication of a positive correlation between clinical improvement and the appearance of delta activity, but there are too few cases to allow a definite statement.

TABLE III.

Percentage of records, at different times, in which delta and theta activity was present.

	Before operation	Time after operation						
		1 day	10 days	3 weeks	6 weeks	3 months	6 months	1 year
Delta ..	0	57	57	36	15	17	19	0
Theta ..	15	64	85	58	58	64	65	60

On the other hand, the volume of gastric secretion under the influence of 1 mg. prostigmin (without test-meal) showed significant differences pre- and post-operatively, as seen on the histogram in fig. 1. The volume of gastric juice became considerably increased post-operatively, but it is noteworthy that no increase in the HCl production occurred.

In commenting on those results, it may be recalled that gastric activity has been described as consisting of three phases. First the cephalic phase, denoting psychogenic influences on the vagus. That the described findings are not of psychogenic nature is supported by the fact that they are independent of the therapeutic result of the operation.

Secondly, the so-called vagus phase: it is known that the vagus exerts its influence on the oxyntic cells, causing discharge of HCl, and that during the vagus phase of gastric activity, the gastric flow is increased; this is the so-called vagus juice. The chemical transmitters to the oxyntic cells are acetylcholine and histamine. Fulton pointed out that according to Messimy and Clifton, the ablation of the frontal association areas in monkeys (areas 9, 10, 11 and 12) causes increased gastric motility, and hyperactivity of the stomach, apparently as a result of increased autonomic activity, "The effects however tend to pass off with time." The findings which have been given are thus well in accordance with the experimental observations on animals. It is possible that part of the orbitofrontal cortex, where autonomic functions are located, becomes isolated by the low vertical incision. It is known that there is an overlapping of the sympathetic and parasympathetic systems in their cortical integration, and it would therefore seem to be not unlikely that the cholinergic activities described may be only a part of the autonomic changes which may later be found.

The third phase of gastric activity, induced by the vagus phase, is chemogenic, acetylcholine being the transmitter of the nervous impulses. It is of interest therefore that although prostigmin preserves the naturally liberated acetylcholine, no significant changes were found regarding the HCl content after prostigmin injection. It may be that although acetylcholine plays a lesser part in the production of HCl than does histamine, it still functions as a powerful activator of the vagus juice production. Further analysis of the third, or chemical phase of gastric activity is not within the scope of the present paper.

In a previous report it was demonstrated that in about two months after leucotomy an increased autonomic homeostasis seems to be established as seen by the patients' resistance to drugs which normally upset the autonomic balance. By this time the indirect cortico-hypothalamic degeneration is probably well established. Thus it may be that the transient autonomic changes described here have a cortical rather than a hypothalamic basis.

It is not justifiable to theorise on such a limited number of experimental observations, however encouraging the mathematical analyses may be. It would, however, seem that the results though as yet incomplete call for further investigations.

I wish to express my thanks to Dr. E. Cunningham Dax for his suggestions and criticisms; to Dr. F. Kraupl and Mr. W. A. Hulme for their technical help.

REFERENCES

DAX, E. C., and RADLEY-SMITH, E. J. (1946) *Proc. R. Soc. Med.*, 39, 448.
FULTON, J. (1943) Physiology of the Nervous System. London.
REITMAN, F. (1945) *J. ment. Sci.*, 91, 318.

Dr. M. B. Brody: The chief experimental finding from the psychological viewpoint is that prefrontal leucotomy does not impair capacity to perform mental tests. In the few papers which record mental test results unimpaired ability has been found mental physiology indicated and post-leucotomy autopsies confirmed the indirect connexions of the prefrontal lobes to the diencephalic centres. Furthermore, it has been established that the highest neural integration of autonomic functions lies in the cortex itself. Therefore it seems reasonable to suppose that partial severance of the thalamo-frontal radiation will induce alteration in autonomic balance. This report deals with changes in the parasympathetic functions as evidenced by the study of the influence of the vagus on gastric functions.

Nine cases have been selected for this report, all of which had pre-operative test meal curves within normal limits. All the cases underwent bilateral, low, vertical leucotomy, by the method which Dax and Radley-Smith (1946) reported to this Society. We believe that by this means fibres from the orbital surface of area 11 as well as from area 12 are amongst those severed.

Each case, when selected for operation had three test meals and each analysis was performed independently by two investigators. The average of the 3 test meal curves was taken as the "pre-operative curve" for each patient. It was hoped that by this method, any emotional factors which influenced the patients' test meal curves would be eliminated whilst the independent titration of two operators would remove reading errors. Similar procedures took place three, five, seven, and ten weeks after leucotomy.

A second group of investigations comprised the analysis of test meals taken under the influence of 1 mg. i.v. prostigmin, pre- and post-operatively, at about three, five, seven and ten weeks' intervals. In a third group of experiments gastric analysis was made after administering 1 mg. i.v. prostigmin alone. In each case the analyses were repeated and the results calculated from the mean of the readings.

The histogram (fig. 1) shows the pre- and post-operative test meal curves. After leucotomy the total acidity is slightly increased, the maximum of the total acidity is reached earlier than pre-operatively, and the emptying time is shortened. The significance of the differences between the pre- and post-operative curves was statistically significant. It should be added that the enumerated differences are already apparent three weeks post-operatively, and are increased at the five-weekly period but that the seven-week curves are less marked and the ten-week curves approximate uniformly to the pre-operative values. The total acidity under the influence of 1 mg. prostigmin if followed by a test meal did not show statistically significant changes.

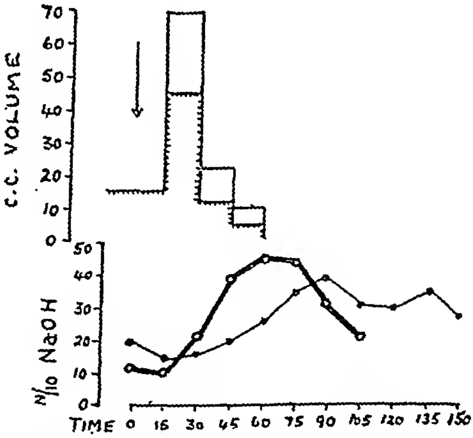


FIG. 1.—Above: Volume of gastric juice after 1 mg. i.v. prostigmin injected at arrow. Pre-operative, dotted line; post-operative, straight line. Below: Test meal curves. Pre-operative, thin line; post-operative, thick line. All amounts are calculated as averages (from 9 cases).

Section of Endocrinology

President—L. R. BROSTER, O.B.E., M.Ch.

[*November* 29, 1946.]

Chromophobe Adenoma in a Male Aged 15½ Years.—S. LEONARD SIMPSON, M.D., and A. DICKSON WRIGHT, M.S.

H. R., now aged 15½ years. At age 13½ while in Australia, suffered from headaches, ophthalmoplegia and later blindness in right eye, with optic atrophy. Left eye showed ptosis, partial optic atrophy and partial temporal hemianopia. Pituitary fossa was considerably enlarged (19 × 21 mm.). Puberty was said to have commenced at 13 but voice was not broken. General condition was one of weakness, apathy and adiposity.

Operation (A. D. W.) June 1945.—The adenoma had extended downwards into the sphenoidal fissure and posteriorly, elevating the optic chiasma. A large amount of necrotic tissue was removed. Histology showed chromophobe adenoma.

Recovery uneventful. A course of X-ray treatment was given because removal of tumour is often incomplete in such cases. Full movements returned to left eye and partial movements to right eye which, however, is still blind.

Result.—Improvement in degree of ophthalmoplegia, but patient weak, apathetic and bedridden, with no appetite and no volition. Testosterone advised (S. L. S.), 25 mg. daily by injections. Increased appetite and strength and sense of well-being. There was also an erotic effect. Up and about. A dramatic manifestation of the effect of testosterone on appetite, well-being, nitrogen retention and muscular strength.

A subcutaneous implantation of 400 mg. testosterone propionate is contemplated.

Chromophobe Adenoma in a Male Aged 67 Years.—S. LEONARD SIMPSON, M.D., and JULIAN TAYLOR, O.B.E., M.S.

In 1934 anæmia, loss of libido, and dyspnœa. In 1940, diminished vision right eye, and headache. Dr. F. W. Price suggested pituitary tumour and referred patient to Dr. F. M. R. Walshe, who diagnosed chromophobe adenoma. X-ray showed great enlargement of sella turcica.

Operation (J. T.) May 1940.—Right transfrontal approach. Intradural. Soft tumour sucked out. Histology showed chromophobe adenoma. One month later seen by S. L. S., complaining of weakness, sensitivity to cold, no libido. Facial hair and pubic hair slight, and axillary hair absent. Pallor. B.P. 90/60. Responded moderately at different periods to desoxycortone, thyroid, and pituitary adrenocorticotrophic hormone; and dramatically to methyl testosterone, 10 mg. under the tongue t.d.s. The patient wrote: "In the very first week there was an enormous improvement in my strength and vitality, and before the end of the first month I felt as I used to feel about twelve years ago before my health first began to deteriorate. I felt thoroughly well and strong, and able to do almost anything without fatigue."

After six weeks a maintenance dose was given of one 5 mg. tablet t.d.s. He was seen in October 1946 when libido, potency and secondary sexual characteristics had returned.

Pituitary Infantilism with Toxic Goitre.—A. W. SPENCE, M.D.

Single woman, aged 23, complaining of failure to grow, absence of periods, palpitations. Delayed growth particularly noticed at 14. Aged 16, given thyroid tablets because of primary amenorrhœa; these were stopped after six months on account of loss of weight, exophthalmos and palpitations. Condition practically unchanged. During past two years has had fortnightly injections of gestyl (pregnant mare's serum extract).

almost without exception. At Runwell Hospital, I tested patients before, and six weeks, four months, one year and two years after operation with a Vocabulary, Terman-Merrill, a modified Babcock, Porteus, Passalong, Kohs', Matrices, Shipley-Hartford, and a variety of sorting tests. Although I cannot present a detailed analysis of the data, I am satisfied that the results showed no impairment. In fact, I therefore abandoned my original project of testing at yearly intervals indefinitely. I next concentrated on investigations with tests of the Goldstein type. These were given at the same intervals as the intelligence tests, and again the results were negative.

This unexpected preservation of mental test ability raises the question: "What part does the prefrontal area play in the so-called higher intellectual processes?" Apparently none, or no indispensable part. On what areas of the brain then, do these functions depend? The most probable answer is on some kind of integrated activity of the cortex as a whole. But one must also consider whether areas other than the cortex are important, and in this connexion it has already been suggested that the true dementia of Pick's disease is associated with changes in the dorso-medial nucleus of the thalamus. The answer to such fundamental problems can be reached by studying prefrontal leucotomy not in isolation but as part of a study of all conditions involving organic brain changes, a study which calls for close co-operation between clinicians, neuro-histologists and psychologists using, as Dr. Meyer has said, a largely standardized technique of examination.

Amongst the patients were some who outside the test sessions showed lack of spontaneity—whose spontaneous ideation and activity did not reach the intellectual level and quality proved by the tests to be within their capacity. Clearly, the test situation, the act of setting a specific task to be done there and then under the examiner's eye, evokes some driving or urging power which is not spontaneously evoked, and is presumably non-cognitive in character. With this observation I wish to couple the clinical observation that after leucotomy, ideas which were formerly held with great emotion may remain unchanged after operation, but stripped of the emotion; and that this fading of the emotion often precedes fading of the ideas themselves.

These observations raise fundamental problems about the nature and genesis of ideation, and the relation of ideation to emotion. We need to know more of the relation of ideation to gnosis, praxis, and to those capacities which are impaired in aphasia, agraphia, alexia, acalculia, &c. Even the relation of ideation to perception is debatable, as may be realized by comparing the seemingly opposite views of Madison Bentley and Bartlett. Apropos the relation of ideation to emotion, Porteus and Kepner point out that although we are accustomed to talk of "ideas and their accompanying emotions", that is, we regard ideation as primary and the emotion as a consequent secondary feature, the truth may be that emotion is the primary state and ideation secondary, that is, that ideation is intellectualization of a primary emotional state. They renewed interest in this old problem because they found that subjects after leucotomy displayed certain changes in performing Porteus Mazes for which the explanation lies, they believe, in the emotional rather than cognitive field.

Pan-Hypopituitarism.—R. S. Bruce Pearson, D.M.

C. R., male, aged 36. First seen December 1944, complaining of breathlessness, lack of energy, hot flushes, spasmodic jerkings of the body. Symptoms present since October 1942 in Palestine when he had a severe pyrexial illness associated with headache, lasting a week. Then severely anæmic with low B.P.

On examination (October 1942).—Face and body hairless—skin soft and dry. Shaved once weekly. Features expressionless and voice toneless. Impotent. Some œdema of legs. Pale, but Hb. 88% (Haldane). Well covered. B.P. below 100 systolic.

Further investigations confirmed pan-hypopituitarism.

Since this time has received treatment with a variety of endocrine preparations with considerable subjective improvement, increased growth of hair and the return of normal sexual activity.

Case for Diagnosis. ? Diabetes Mellitus with Diabetes Insipidus.—A. C. Crooke, M.D.

Sylvia M., aged 10 years.

December 1940, aged 4 years, onset of diabetes mellitus. This has been well controlled by diet and insulin (20-32 units globin insulin daily).

She had not attended the clinic for five months but three months ago she developed excessive thirst and began passing large quantities of urine, although her mother, who tested the urine daily, said it was usually sugar-free and she occasionally had slight symptoms of hypoglycæmia. Mother tried to prevent her drinking, but she would run away to shops and ask for water. Otherwise very well; no relevant family history of previous illnesses.

On examination, 31.9.46.—No abnormal physical signs. Only slight glycosuria and no acetone.

Admitted to hospital: Slight pyrexia which has since persisted. Catheter specimen of urine: Coliform organisms cultured, no pus, no other cause for pyrexia found. X-rays chest and skull normal. Began to show marked glycosuria; insulin increased progressively to 100 units soluble in 3 divided doses daily. Glycosuria now fairly well controlled again; still frequency of micturition (15-25 times day, 3-8 times night); 5-11 pints in twenty-four hours.

Basophilism Treated Unsuccessfully with Massive Doses of Oestrogens and Deep X-ray Therapy, but Cured by Radon Seeds Inserted into the Sella Turcica.—A. C. Crooke, M.D.

Maud F., married, aged 30, admitted to London Hospital 26.5.40. Her only child had been born eight months previously. Two months later weight began to increase rapidly and broad purple striæ atrophicæ appeared on abdomen. Excess of hair developed on upper lip. Face became bloated and bluish-red, skin greasy. Periods became irregular and finally ceased. Moderate cervicodorsal kyphosis.

When first seen B.P. 150/70; subsequently lower. Diabetic sugar tolerance curve. Deep X-ray treatment by Dr. Jupe, of 1,000 r in twenty-two days. Condition deteriorating rapidly; transferred to Mr. Northfield. 14.10.40: Two radon seeds, each of 1·5 millicuries, inserted into pituitary gland. Within nine days face less bloated, bluish tinge disappeared. Abdominal striæ pale pink.

After discharge complained of fatigue and great muscular weakness. Lost 3½ st. in weight. Subsequently gained 1 st.

It was considered that she was suffering from a degree of pituitary insufficiency, but she gradually recovered and all her symptoms disappeared, except that her menstruation has been very irregular with long periods of amenorrhœa.

Father 5 ft. 4 in. Mother 5 ft. Heights of four adult brothers range from 5 ft. 5 in. to 5 ft. 10 in.; of three adult sisters from 5 ft. 2 in. to 5 ft. 6 in.

On examination.—Height 4 ft. 6 in., weight 5 st. 9 lb. Appears ten years younger than her age. Co-operative, composed, intelligent. Infantile configuration and development: mild oxycephaly, well covered, not obese, breasts poorly developed, pigmented nipples, no axillary hair, pubic hair scanty. Infantile vagina, hyperextensibility of joints and mild pes planus. Moderate exophthalmos with lid retraction and slight lid lag. Slight tremor of hands. Thyroid moderately enlarged. Heart normal; pulse (day) 120-140, (night) 80-90. B.P. 165/95. E.C.G. sinus tachycardia. Hb. 90%. W.B.C. 5,000. B.M.R. + 33%. Blood cholesterol 112 mg. per 100 c.c. X-rays: Pituitary fossa 9 × 6 mm. Wrists: Non-fusion of epiphyses and decalcification. Urinary excretion of 17-ketosteroids: 5 mg. in twenty-four hours.

Dr. V. C. Medvei: The case presented certain difficulties. My Chief, Dr. Spence, encouraged me to offer an alternative attempt at explanation.

(1) The hypopituitarism is not quite typical; the blood-pressure has always been rather high.

(2) The exophthalmos became noticeable after thyroid administration, but it may have begun two years before that.

(3) The condition has not changed for the last two and a half years, and the pulse-rate comes down to 72 while she is asleep.

(4) X-ray evidence of a delayed ossification is not usual in pituitary dwarfism beyond the age of 21. In thyroid disorders delayed ossification is significant for juvenile myxœdema.

(5) A deformity of the skull is present. Schueller pointed out combination between acrocephaly, chondrodystrophy and other forms of dwarfism. J. Bauer found a combination of acrocephaly and exophthalmos often concurrent. Thomas described a girl of 1½ years with acrocephaly, enlarged sella and exophthalmos. In 1924 a young girl of 15 was referred to J. Bauer with exophthalmos and signs of hyperthyroidism as an exophthalmic goitre. She belonged to a similar group that was first described by Crouzon in 1912 as a cranio-facial dysostosis.

BIBLIOGRAPHY

Bauer, J. (1924) Konstitutionelle Disposition, 3rd edition. Berlin. p. 332.
Crouzon, O. (1912) *Bull. Soc. méd. Hôp. Paris*, 33, p. 545.
Schueller, A. (1915) *Fortschr. Röntgenstr.*, 23, 12.
Thomas, E. (1914) *Z. Kinderheilk.*, 10, 109.

Long-standing Hypopituitarism with Recent Signs Suggesting Either Chromophilic Adenoma or Suprasellar Tumour.—H. S. Le Marquand, M.D.

Female patient, aged 28 years.

History.—Birth-weight 7½ lb. Developed normally until the age of 8 years when diabetes insipidus occurred. This cleared spontaneously at 11 years.

November 1938: First seen, aged 20. Measurements: Head 20·5 in. (= age of 6½ years); height 55·5 in. (= age of 11 years); weight 75 lb. (= age of 11½ years).

X-rays: Epiphyseal development retarded by two years. Pituitary fossa at upper limit of normal size. Small stature and development. Fine wrinkled skin, undeveloped breasts, amenorrhœa.

Diagnosis: Hypopituitarism.

1942: When examined by gynæcologist under anæsthesia all that could be felt of internal genital organs was a minute cervix. During eight years of observation has been treated with thyroid gland, various pituitary preparations and with œstradiol. Menstrual bleeding while under treatment with œstradiol. Has grown ¾ in. and put on 15 lb. Mammary glands have developed. Pubic hair present. June 1946: Aged 28. Complained of loss of vision of right eye. Mr. Cashell reported: "Slight constriction of R. field of vision, slight pallor of R. disc." Vision L. and R. 6/6. Dr. Cave reported: "Pituitary fossa enlarged, posterior clinoid process thin." September 1946: Course of deep X-ray therapy to pituitary gland. October 1946: Mr. Cashell reports: "There is optic atrophy of the R. disc, the loss of central fixation is due to a R. hemianopic scotoma which has affected the macular bundle. Lesion is increasing and there is a suggestion of a L. temporal defect. Vision R. 6/60. L. 6/6."

Pan-Hypopituitarism.—R. S. Bruce Pearson, D.M.

C. R., male, aged 36. First seen December 1944, complaining of breathlessness, lack of energy, hot flushes, spasmodic jerkings of the body. Symptoms present since October 1942 in Palestine when he had a severe pyrexial illness associated with headache, lasting a week. Then severely anæmic with low B.P.

On examination (October 1942).—Face and body hairless—skin soft and dry. Shaved once weekly. Features expressionless and voice toneless. Impotent. Some œdema of legs. Pale, but Hb. 88% (Haldane). Well covered. B.P. below 100 systolic.

Further investigations confirmed pan-hypopituitarism.

Since this time has received treatment with a variety of endocrine preparations with considerable subjective improvement, increased growth of hair and the return of normal sexual activity.

Case for Diagnosis. ? Diabetes Mellitus with Diabetes Insipidus.—A. C. Crooke, M.D.

Sylvia M., aged 10 years.

December 1940, aged 4 years, onset of diabetes mellitus. This has been well controlled by diet and insulin (20-32 units globin insulin daily).

She had not attended the clinic for five months but three months ago she developed excessive thirst and began passing large quantities of urine, although her mother, who tested the urine daily, said it was usually sugar-free and she occasionally had slight symptoms of hypoglycæmia. Mother tried to prevent her drinking, but she would run away to shops and ask for water. Otherwise very well: no relevant family history of previous illnesses.

On examination, 31.9.46.—No abnormal physical signs. Only slight glycosuria and no acetone.

Admitted to hospital: Slight pyrexia which has since persisted. Catheter specimen of urine: Coliform organisms cultured, no pus, no other cause for pyrexia found. X-rays chest and skull normal. Began to show marked glycosuria: insulin increased progressively to 100 units soluble in 3 divided doses daily. Glycosuria now fairly well controlled again; still frequency of micturition (15-25 times day, 3-8 times night): 5-11 pints in twenty-four hours.

Basophilism Treated Unsuccessfully with Massive Doses of Oestrogens and Deep X-ray Therapy, but Cured by Radon Seeds Inserted into the Sella Turcica.—A. C. Crooke, M.D.

Maud F., married, aged 30, admitted to London Hospital 26.5.40. Her only child had been born eight months previously. Two months later weight began to increase rapidly and broad purple striæ atrophicæ appeared on abdomen. Excess of hair developed on upper lip. Face became bloated and bluish-red, skin greasy. Periods became irregular and finally ceased. Moderate cervicodorsal kyphosis.

When first seen B.P. 150/70; subsequently lower. Diabetic sugar tolerance curve. Deep X-ray treatment by Dr. Jupe, of 1,000 r in twenty-two days. Condition deteriorating rapidly; transferred to Mr. Northfield. 14.10.40: Two radon seeds, each of 1·5 millicuries, inserted into pituitary gland. Within nine days face less bloated, bluish tinge disappeared. Abdominal striæ pale pink.

After discharge complained of fatigue and great muscular weakness. Lost 3½ st. in weight. Subsequently gained 1 st.

It was considered that she was suffering from a degree of pituitary insufficiency, but she gradually recovered and all her symptoms disappeared, except that her menstruation has been very irregular with long periods of amenorrhœa.

Primary Hyperplasia of the Parathyroids in a Boy Aged 8 Years.—N. F. ELLIOTT BURROWS, B.M., for W. G. WYLLIE, F.R.C.P.

Three months preceding admission, insidious onset of anorexia, increasing polydipsia with enuresis, occasional vomits and frequent pains in head, abdomen and behind knees. Progressive muscular weakness. Attack of tonsillitis at onset. Measles only other illness. Parents and two siblings healthy.

On examination.—Extreme lethargy and recent weight loss; subsequently nuchal stiffness and frontal headache. Blood-count: R.B.C. 5,280,000; Hb. 85%; C.I. 0·81; W.B.C. 8,900 (polys. 50%). C.S.F. pressure 70 mm. Urine: Acid, Alb. 15 mg.%. Blood urea 35 mg.%. 1 : 1,000 Mantoux very strongly positive. B.P. 95/65.

Course in hospital.—During next five months symptoms continued unabated. No evidence of active Tb. found. No benefit from posterior pituitary extract injection. Intravenous pyelography attempted on three occasions but renal concentration was lacking. Routine agglutination reactions negative. E.S.R. remained around 60 mm. in one hour. ? tuberculoma in floor of fourth ventricle. Normal ventriculogram performed by Mr. Wylie McKissock.

Attention was drawn to skeletal system by appearance of rarefaction in necks of femurs and by necrotic nature of cranial bur holes. Extreme osteoporosis of skull. Urine: Heavy precipitate with Sulkowitch reagent. Blood: Serum calcium 18·8 mg.%. Inorganic phosphorus 2·8 mg.%. Alkaline serum phosphatase 93 units.

Operation (C. Donald).—Exploration of parathyroids. Tumour removed, the size of large hazel nut, purple in colour, inferior to thyroid capsule beneath sternal notch. Histologically diffuse hyperplasia, without evidence of adenomatous arrangement.

Progress.—Immediate amelioration of many symptoms. Fluid intake dropped to 25 oz. daily, no further enuresis. Blood Ca fell in six days to 6·5 mg.%. Alkaline serum phosphatase continued greatly raised. No tetany; level restored by high Ca intake with 10,000 units vitamin D daily. Weight gain of over 4 lb. in less than three weeks; improvement in muscle tone. Progress continuous. Bones show marked improvement. Three weeks after operation blood chemistry revealed: Serum Ca 9·4, Inorganic P. 3·3 mg.%. Alk. S.P. 62 units. On 8.10.46: Serum Ca 10·9, Inorganic P. 3·4 mg.%. Alk. S.P. 14 units.

Precocious Puberty of ? Suprarenal Origin.—N. F. ELLIOTT BURROWS, B.M., for W. G. WYLLIE, F.R.C.P.

John A., aged 5¾ years. Normal birth and babyhood until eighteen months when his genitalia were thought large for his age. Since then he has grown excessively: adult muscular build, pubic hair, enlarged penis, but normal sized testicles.

17-ketosteroids, 20.9.46: 18·4 mg. 4.10.46: 11·4 mg. per day.

23.10.46. Laparotomy by Mr. Twistington Higgins. Left kidney and suprarenal felt normal, right kidney outline nobbly towards upper pole. 6.11.46: Second operation. Right kidney incision with rib resection. Suprarenal enlarged but no localized tumour, the enlargement was diffuse, extending to diaphragm and was separated with difficulty. Suprarenal partly removed in two pieces.

17-ketosteroids. 18.11.46: 5·2 mg. per day. Bone age of boy of 13 years. Skull X-ray normal.

Histological report [Dr. Martin Bodian].—(1) Main piece of gland 3·7 g., (2) subsidiary piece 0·9 g. containing a little yellow nodule.

(1) Normal zonal architecture of cortex with hardly any medullary tissue present. Vine's Ponceau fuchsin reaction negative. No mitotic or multinucleated cells.

(2) Nodule consists of cortical tissue without orderly zonal arrangement and has larger cells than main gland. Histological appearances do not indicate neoplasm or hyperplasia.

Section of Pædiatrics

President—DENIS BROWNE, F.R.C.S.

[*October* 25, 1946]

Kala-Azar in Infancy

By Professor J. E. DEBONO (*Malta*)

ALTHOUGH indigenous leishmaniasis does not occur in England, cases might be, and in fact are, imported from endemic areas. Their very rarity make diagnosis more difficult unless the possibility of the disease and its main features are kept in mind. There is no essential difference between infantile and adult leishmaniasis. The parasite and the pathology are the same and it is more exact to speak of leishmaniasis in infancy. Infection in infants is associated with canine leishmaniasis and is most prevalent in the Mediterranean area. In China older children are affected and in India and the Sudan, adults are attacked. There is no hard and fast rule, however, and it is quite possible for a baby to acquire the disease in an area where the adult form is prevalent. It is important to remember that leishmaniasis is not necessarily a tropical disease and that in Europe itself it could occur in any place south of the latitude of Paris.

"Infancy" in connexion with kala-azar is not to be regarded in its strict sense of the first year of life. In Malta the age distribution of the last 200 cases was as follows:

0 to 1 year ..	10	4 to 5 years ..	20
1 to 2 years ..	76	5 to 6 years ..	8
2 to 3 years ..	55	6 to 7 years ..	2
3 to 4 years ..	26	7 to 8 years ..	3

The youngest patient was 4 months old.

The basic pathological lesion is a marked and universal proliferation of the reticulo-endothelial system. On inoculation by the phlebotomus the flagellate leishmaniæ penetrate reticulo-endothelial cells in the immediate neighbourhood and change into the spherical form known as the "Leishman-Donovan Body" (L.D.B.). Here they multiply and pass on to other R.-E. cells via the minute protoplasmic processes which connect these cells together. In tropical sore the infection remains localized, in visceral leishmaniasis the parasites are disseminated throughout the whole R.-E. system. Probably dissemination occurs through the detachment of infected endothelial cells and their carriage by the circulation to the spleen, liver, bone-marrow, glands and intestines.

Under the stimulus of parasitic invasion both the cells and the reticulum proliferate. The spleen enlarges to a size only rivalled by myelocytic leukæmia; the Malpighian bodies disappear. In the liver the proliferation of Kupffer's cells produce atrophy of the parenchyma. The superficial lymph glands are only moderately enlarged and rarely give rise to diagnostic difficulties. The enlargement is more marked in the tracheo-bronchial and mesenteric groups, but this is probably the result of repeated secondary infections. In the intestines a sheet of infected cells sometimes lines the subserous membrane. Ulcers may form from time to time in the colon and give rise to dysenteric symptoms with passage of blood and mucus.

The most important changes take place in the bone-marrow. The hæmopoietic elements are encroached upon and crowded out by the infected and proliferated R.-E. tissue, producing a condition analogous to aplastic anæmia. The anæmia of leishmaniasis is normocytic and orthochromic. There is no evidence of hæmolysis and no reticulocytosis. The erythrocytes are not injured in any way but their production is seriously interfered with. In ordinary cases the average red count is

Primary Hyperplasia of the Parathyroids in a Boy Aged 8 Years.—N. F. Elliott Burrows, B.M., for W. G. Wyllie, F.R.C.P.

Three months preceding admission, insidious onset of anorexia, increasing polydipsia with enuresis, occasional vomits and frequent pains in head, abdomen and behind knees. Progressive muscular weakness. Attack of tonsillitis at onset. Measles only other illness. Parents and two siblings healthy.

On examination.—Extreme lethargy and recent weight loss; subsequently nuchal stiffness and frontal headache. Blood-count: R.B.C. 5,280,000; Hb. 85%; C.I. 0·81; W.B.C. 8,900 (polys. 50%). C.S.F. pressure 70 mm. Urine: Acid, Alb. 15 mg.%. Blood urea 35 mg.%. 1:1,000 Mantoux very strongly positive. B.P. 95/65.

Course in hospital.—During next five months symptoms continued unabated. No evidence of active Tb. found. No benefit from posterior pituitary extract injection. Intravenous pyelography attempted on three occasions but renal concentration was lacking. Routine agglutination reactions negative. E.S.R. remained around 60 mm. in one hour. ? tuberculoma in floor of fourth ventricle. Normal ventriculogram performed by Mr. Wylie McKissock.

Attention was drawn to skeletal system by appearance of rarefaction in necks of femurs and by necrotic nature of cranial bur holes. Extreme osteoporosis of skull. Urine: Heavy precipitate with Sulkowitch reagent. Blood: Serum calcium 18·8 mg.%. Inorganic phosphorus 2·8 mg.%. Alkaline serum phosphatase 93 units.

Operation (C. Donald).—Exploration of parathyroids. Tumour removed, the size of large hazel nut, purple in colour, inferior to thyroid capsule beneath sternal notch. Histologically diffuse hyperplasia, without evidence of adenomatous arrangement.

Progress.—Immediate amelioration of many symptoms. Fluid intake dropped to 25 oz. daily, no further enuresis. Blood Ca fell in six days to 6·5 mg.%. Alkaline serum phosphatase continued greatly raised. No tetany; level restored by high Ca intake with 10,000 units vitamin D daily. Weight gain of over 4 lb. in less than three weeks; improvement in muscle tone. Progress continuous. Bones show marked improvement. Three weeks after operation blood chemistry revealed: Serum Ca 9·4. Inorganic P. 3·3 mg.%. Alk. S.P. 62 units. On 8.10.46: Serum Ca 10·9. Inorganic P. 3·4 mg.%. Alk. S.P. 14 units.

Precocious Puberty of ? Suprarenal Origin.—N. F. Elliott Burrows, B.M., for W. G. Wyllie, F.R.C.P.

John A., aged 5¾ years. Normal birth and babyhood until eighteen months when his genitalia were thought large for his age. Since then he has grown excessively: adult muscular build, pubic hair, enlarged penis, but normal sized testicles.

17-ketosteroids, 20.9.46: 18·4 mg. 4.10.46: 11·4 mg. per day.

23.10.46. Laparotomy by Mr. Twistington Higgins. Left kidney and suprarenal felt normal, right kidney outline nobbly towards upper pole. 6.11.46: Second operation. Right kidney incision with rib resection. Suprarenal enlarged but no localized tumour, the enlargement was diffuse, extending to diaphragm and was separated with difficulty. Suprarenal partly removed in two pieces.

17-ketosteroids, 18.11.46: 5·2 mg. per day. Bone age of boy of 13 years. Skull X-ray normal.

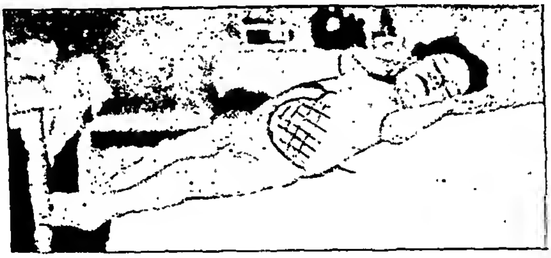
Histological report [Dr. Martin Bodian].—(1) Main piece of gland 3·7 g., (2) subsidiary piece 0·9 g. containing a little yellow nodule.

(1) Normal zonal architecture of cortex with hardly any medullary tissue present. Vine's Ponceau fuchsin reaction negative. No mitotic or multinucleated cells.

(2) Nodule consists of cortical tissue without orderly zonal arrangement and has larger cells than main gland. Histological appearances do not indicate neoplasm or hyperplasia.

temperature chart. The fever in leishmaniasis is made up of a number of short sharp rises or *accesses* of temperature in the twenty-four hours. There is one about 11 a.m., perhaps another rise in the evening and almost invariably a rise at night, followed by sweating in the early hours of the morning. The double and even triple rise of temperature is very suggestive. In its absence the diagnosis must be made by exclusion and confirmed if possible by culture of the parasite from the blood.

In the fully-developed case diagnosis is easier. The appearance is often characteristic. The child is thin, emaciated, looks miserable and suffers from general hypotonia. The abdomen is swollen and shows a marked protuberance either in the left hypochondrium or in the hypogastrium when the child stands up. The facies varies. In dark children there is an almost pathognomonic deep greenish pigmentation of the face and exposed parts. Fair children develop a marked pallor, which together with the slight generalized œdema suggests subacute nephritis (*see* fig.).



The spleen at this stage is often enormously enlarged reaching down into the left iliac fossa and crossing over to the right half of the abdomen. It is firm but not hard and there is no tenderness unless there has been recent infarction. With considerable enlargement and hypotonic muscles, ptosis of the spleen is almost invariable, hence the pendulous and protuberant abdomen.

The disease has to be differentiated from the long list of conditions which produce splenomegaly in children. Careful clinical examination and repeated examination of the blood enable one to eliminate the majority of these including malaria. In young babies the possibility of congenital syphilis has to be considered. In Malta the diagnosis is complicated by the frequency of undulant fever, but in this disease the spleen never attains the size it reaches in kala-azar.

The decisive test—to be carried out in all cases before treatment is started—is the demonstration of the leishmaniæ. This is best done by splenic puncture. Many tests and procedures have been devised to avoid the risks of this supposedly dangerous operation, but none could compare with it as regards reliability. The aldehyde, the antimony and Ray's tests are not usually positive before the fourth month and they may be positive in other conditions. The complement-fixation test is still in its infancy. Blood culture requires a meticulous technique and at best is positive in only 70% of the cases. Bone-marrow, liver and gland puncture have been suggested and used as alternatives. Of these tibial puncture is probably the best, but in my opinion it is more dangerous and certainly more painful than splenic puncture. The most important point, however, is that it is often negative when the splenic juice is teeming with parasites.

Splenic puncture is simple, and when performed with proper precautions is practically devoid of danger. In my experience extending over 2,000 cases there has

2,500,000 per c.mm., but in severe and advanced cases it may be as low as 1,000,000 per c.mm. The myelocytic tissue suffers to an even greater extent and leucopenia is a prominent feature of leishmaniasis. In advanced cases the leucocytes are often reduced to 2,000 per c.mm. or even less. The granulocytes are chiefly affected and a condition tantamount to agranulocytosis may occur. This neutropenia is no doubt responsible for the great liability to secondary infections and the occurrence of cancrum oris. There is a relative as well as an absolute monocytosis. The megakaryocytes are reduced to vanishing point and in the circulation the platelets may fall to 100,000 or under. This thrombocytopenia results in a tendency to hæmorrhages, purpura and ecchymoses.

The plasma shows marked alterations of which the most important is a fall in the albumen and a rise in the globulin fraction. The changes in the plasma are the basis of a number of diagnostic tests and produce an accelerated sedimentation rate. The fall in the albumen level together with the low hæmoglobin are responsible for the œdema commonly seen in advanced cases.

The clinical picture is a reflection of the underlying pathology. The incubation period is long, corresponding to the slow invasion and dissemination. It is usually stated to be between three and four months, but longer periods occur. If one added the latent period between the first symptoms and the full development of the disease eighteen to twenty-four months might easily elapse, and the possibility of such a prolonged incubation has to be considered in investigating the history. The onset of kala-azar is usually insidious with slight irregular fever and a gradual loss of appetite, colour, weight and energy. As these symptoms occur at a time of life when trivial complaints are common, they are often neglected and it may be months before the real nature of the disease is recognized. Occasionally, and more frequently in children under 2 years, the onset is acute with hyperpyrexia, chills and vomiting. The initial febrile period lasts two to six weeks and constitutes the first "wave". This is followed by an intermission—the so-called "latent period" which lasts another two to six weeks but can be much longer. Thereafter the fever rises again and the spleen begins to enlarge and continues to do so at the rate of two to three fingerbreadths per month.

Untreated leishmaniasis in infants is invariably fatal. The course could be acute, subacute or chronic. Acute leishmaniasis is commoner in young babies. It is characterized by a violent onset, high continuous fever, and rapid but moderate enlargement of the spleen. There is no latent period and death occurs in three to four months. The majority of cases in Malta run a subacute course lasting six to eighteen months: the trend is progressively downwards with persistent fever, increasing splenomegaly and progressive anæmia and cachexia. It is punctuated by alternating attacks of diarrhœa and bronchitis. The disease may be cut short by a fatal attack of bronchopneumonia or by the development of cancrum oris. Otherwise the child dies of marasmus and exhaustion. Sudden and unexpected death sometimes occurs even in children, who are apparently improving under treatment. It is heralded by hyperpyrexia, vomiting, rapid pulse, intense dyspnœa, cyanosis and extensive hæmorrhages under the skin. The picture is reminiscent of acute suprarenal hæmorrhage.

In older children the disease sometimes runs a chronic course lasting for two or more years with periods of almost total recovery, in which the only symptom is the splenomegaly. According to some Continental authors many of these cases recover spontaneously.

The diagnosis of leishmaniasis before the spleen is definitely enlarged is very difficult and often is only made retrospectively. At this stage leishmaniasis presents itself as a fever of unknown origin The leucopenia is helpful but the most important clue is afforded by an analysis of the temperature by means of a two- or four-hourly kala-azar in infants would have served equally well for that disease when seen in India in infants and it would seem, therefore, that in either case we deal with the same clinical entity.

As a possible explanation of this difference in the two areas I would like to advance a tentative hypothesis in the hope that it may raise some discussion among those familiar with this disease. We know that in the Mediterranean area kala-azar is essentially a disease of dogs and that man (infants and young children) is more or less accidentally infected, whereas in India the disease in dogs is at present unknown. In infected dogs the skin often harbours the parasite in very large numbers and is a rich source of infection for the carrier sandflies.

The very considerable percentage of infected dogs in close association with children in the Mediterranean area would result in most of the children in such areas being repeatedly infected with small doses of leishmania parasites from sandflies which had previously fed on the dogs. In some of these children, owing to a large dose of parasites on some occasion, or for some other reason, the disease might manifest itself as a frank case of kala-azar. In the others the repeated dosage with parasites might build up an immunity which could be maintained by a low grade and inapparent infection in the skin so that in later life they would be immune. Such a train of events would be a possible explanation of the comparative rarity of the disease in adults. In India, on the other hand, where no animal reservoir is known this same immunity would not be built up and therefore older children and adults would be fully susceptiole to infection. Corroboration is lent to this theory by the fact that in the Mediterranean area adults coming from non-endemic areas, such as troops from Great Britain, appeared to be much more susceptible than adults of the local population.

With regard to diagnosis by spleen puncture I was glad to hear that Professor Debono finds spleen puncture the best and most reliable method of diagnosis and considers it much superior to sternal puncture. This has been our experience in India and I am glad to have it confirmed by Professor Debono from Malta because, for some reason, there is the greatest reluctance in this country in employing spleen puncture on account of the supposed risky nature of the operation. In actual fact, as proved on thousands of cases in India, the operation, properly performed, carries little risk and is the most effective means of diagnosis in this disease.

Three points occur to me for discussion: In certain villages in Greece a considerable number of cases of kala-azar in infants have been of a hæmorrhagic type; that is to say, the skin of these infants has shown small hæmorrhages almost covering the body whilst in neighbouring villages the disease has been present without this phenomenon.

Secondly, statements have been made by some workers that the pentavalent antimony preparations are less effective in Mediterranean kala-azar than in Indian as evidenced by the greater quantities of those drugs required for cure and the marked tendency to relapse.

Lastly, has Professor Debono come across any cases of the condition which has been described in India under the name Dermal Leishmanoid?

Professor Debono (in reply): Colonel Shortt's theory regarding the different age incidence in Malta and India is very attractive. The only difficulty is that mild and abortive forms have not been met with in children. We have not seen any special hæmorrhagic type of kala-azar. Petechiæ and hæmorrhages occur in advanced and neglected cases. In spite of a check-up on all our old cases, going back to a period of ten years, no signs of anything resembling Dermal Leishmanoid were noted.

[*November* 22, 1946]

Thyrotoxicosis in a Child Aged 2 Years 9 Months.—GERALD SLOT, M.D.

Bessie E. Six months ago parents began to notice that the child's eyes were becoming more prominent, the condition becoming gradually more obvious since then. She has been otherwise normal except that she has had some diarrhœa and has not been gaining weight.

Previous history.—Pneumonia when aged 1 year.

Family history.—No family history of goitre. Both parents healthy. One other child, aged 5 months, appears normal.

On examination.—Normal intelligence. Marked bilateral exophthalmos. All eye signs for exophthalmos. Diffuse enlargement of thyroid gland, smooth surface. Right lobe larger than left. Tremor of fingers on stretching out arms. Sleeping pulse average 120. Heart: within normal limits, heart sounds normal.

Investigations.—X-ray skull: No gross abnormality, pituitary fossa normal. X-ray chest normal, no retrosternal goitre. Blood cholesterol 135 mg. per 100 c.c. W.R. and Khan negative. Blood-count: Hb. 88%; W.B.C. 6,000; normal differential. E.C.G. shows tachycardia. B.M.R. not possible owing to patient's age. Rough been two fatalities—one in a child suffering from leukæmia and the other in a moribund patient.

The specific treatment of infantile leishmaniasis was introduced by Caronia of Catania in 1914. The sodium-antimony tartrate used originally has been substituted by pentavalent organic antimony compounds, which are equally effective but less toxic. There are a large number of these preparations each with its own advocates and enthusiasts, but I think success depends more on the scheme of treatment and on attention to details than upon the drug itself. Before the war Neostibosan was used, but since 1940 Neostam—the only preparation that could be obtained at the time—has been employed with very satisfactory results. In the last series of 200 cases there has been 3 deaths and 7 relapses, a result which compares well with those obtained in other clinics. Stilbamidine, a different kind of preparation, which has proved very effective in the resistant Sudan kala-azar was ineffective when tried in Malta, and its use had to be abandoned on account of the severe toxic reactions.

Most of the patients in Malta were treated as out-patients. The injections were given three times a week on alternate days. It was found that the intensive treatment by daily injections was not suitable for children. It upset them too much and was often followed by relapses. The injections were always given intravenously, in young infants in the jugular vein. This presented no special difficulty. Absorption after intramuscular injection was often irregular and in many cases the drug failed to reach a sufficient concentration in those situations where it was needed. The result was the development of antimony fastness on the part of the leishmaniæ, with persistence of the infection or an early relapse. When intramuscular Neostibosan was the standard treatment the relapse rate was as high as 20%.

It was impossible to calculate the dose according to the weight as young children required proportionately more than older ones. The following plan was therefore adopted. The initial dose was 0·05 gramme. This was increased by another 0·05 gramme (or 0·025 gramme in the case of infants under 1 year and debilitated patients) until the limit of tolerance, shown by immediate vomiting, was reached. The average dose was 0·10 gramme to 0·15 gramme in babies under 1 year, 0·2 gramme to 0·25 gramme in those under 2 years and 0·3 gramme in older children. The treatment consisted of 16 injections. The full course was given even if improvement was immediate. On the other hand no attempt was made to exceed this number of injections even if the spleen remained large. In most cases the splenomegaly receded without further treatment. If after two months the spleen was still large and L.D.B.s were still present, another course, with a slightly higher dosage was given. Increasing the number of injections or starting a new course before the end of two months was followed in most cases by signs of antimony poisoning.

Adjuvant treatment is of the greatest importance. Hospitalization is avoided as much as possible to avoid secondary infections. Iron and vitamin supplements were given in all our cases. Strict oral hygiene was insisted upon to avoid the development of cancrum oris. Blood transfusions were given whenever the hæmoglobin fell under 40%. Penicillin has no specific effect on the leishmaniasis itself, but it has proved invaluable in the treatment of intercurrent bronchopneumonia and together with blood transfusion was life-saving in the case of cancrum oris.

Colonel H. E. Shortt, I.M.S.: I would like to draw attention to the word "infancy" in the title of Professor Debono's paper. Why should kala-azar be so predominantly a disease of infants in the Mediterranean area as compared with kala-azar in the East, and especially in India, where the disease is relatively uncommon in infants? Thus in India the percentage of cases in children under 1 year old is 0·06 whereas in the Mediterranean area 10 to 11% of cases are in children at the breast and over 60% of cases are in children up to 2 years old. On the other hand Indian kala-azar is a disease of older children and young adults, while the Mediterranean form is comparatively rare among adults. In spite of these differences the clinical picture drawn by Professor Debono of kala-azar in infants would have served equally well for that disease when seen in India in infants and it would seem, therefore, that in either case we deal with the same clinical entity.

As a possible explanation of this difference in the two areas I would like to advance a tentative hypothesis in the hope that it may raise some discussion among those familiar with this disease. We know that in the Mediterranean area kala-azar is essentially a disease of dogs and that man (infants and young children) is more or less accidentally infected, whereas in India the disease in dogs is at present unknown. In infected dogs the skin often harbours the parasite in very large numbers and is a rich source of infection for the carrier sandflies.

The very considerable percentage of infected dogs in close association with children in the Mediterranean area would result in most of the children in such areas being repeatedly infected with small doses of leishmania parasites from sandflies which had previously fed on the dogs. In some of these children, owing to a large dose of parasites on some occasion, or for some other reason, the disease might manifest itself as a frank case of kala-azar. In the others the repeated dosage with parasites might build up an immunity which could be maintained by a low grade and inapparent infection in the skin so that in later life they would be immune. Such a train of events would be a possible explanation of the comparative rarity of the disease in adults. In India, on the other hand, where no animal reservoir is known this same immunity would not be built up and therefore older children and adults would be fully susceptible to infection. Corroboration is lent to this theory by the fact that in the Mediterranean area adults coming from non-endemic areas, such as troops from Great Britain, appeared to be much more susceptible than adults of the local population.

With regard to diagnosis by spleen puncture I was glad to hear that Professor Debono finds spleen puncture the best and most reliable method of diagnosis and considers it much superior to sternal puncture. This has been our experience in India and I am glad to have it confirmed by Professor Debono from Malta because, for some reason, there is the greatest reluctance in this country in employing spleen puncture on account of the supposed risky nature of the operation. In actual fact, as proved on thousands of cases in India, the operation, properly performed, carries little risk and is the most effective means of diagnosis in this disease.

Three points occur to me for discussion: In certain villages in Greece a considerable number of cases of kala-azar in infants have been of a hæmorrhagic type; that is to say, the skin of these infants has shown small hæmorrhages almost covering the body whilst in neighbouring villages the disease has been present without this phenomenon.

Secondly, statements have been made by some workers that the pentavalent antimony preparations are less effective in Mediterranean kala-azar than in Indian as evidenced by the greater quantities of those drugs required for cure and the marked tendency to relapse.

Lastly, has Professor Debono come across any cases of the condition which has been described in India under the name Dermal Leishmanoid?

Professor Debono (in reply): Colonel Shortt's theory regarding the different age incidence in Malta and India is very attractive. The only difficulty is that mild and abortive forms have not been met with in children. We have not seen any special hæmorrhagic type of kala-azar. Petechiæ and hæmorrhages occur in advanced and neglected cases. In spite of a check-up on all our old cases, going back to a period of ten years, no signs of anything resembling Dermal Leishmanoid were noted.

[*November* 22, 1946]

Thyrotoxicosis in a Child Aged 2 Years 9 Months.—GERALD SLOT, M.D.

Bessie E. Six months ago parents began to notice that the child's eyes were becoming more prominent, the condition becoming gradually more obvious since then. She has been otherwise normal except that she has had some diarrhœa and has not been gaining weight.

Previous history.—Pneumonia when aged 1 year.

Family history.—No family history of goitre. Both parents healthy. One other child, aged 5 months, appears normal.

On examination.—Normal intelligence. Marked bilateral exophthalmos. All eye signs for exophthalmos. Diffuse enlargement of thyroid gland, smooth surface. Right lobe larger than left. Tremor of fingers on stretching out arms. Sleeping pulse average 120. Heart: within normal limits, heart sounds normal.

Investigations.—X-ray skull: No gross abnormality, pituitary fossa normal. X-ray chest normal, no retrosternal goitre. Blood cholesterol 135 mg. per 100 c.c. W.R. and Khan negative. Blood-count: Hb. 88%; W.B.C. 6,000; normal differential. E.C.G. shows tachycardia. B.M.R. not possible owing to patient's age. Rough test by Reed's formula + 54. Weight: 7.10.46, 1 st. 9 lb. 12 oz. 8.11.46, 1 st. 7 lb. 3 oz.

Treatment.—Methyl thiouracil 0·1 gramme q.i.d. for three days, started on 7.11.46. Thereafter 0·1 gramme t.d.s.

POSTSCRIPT (18.2.47).—The child was discharged from hospital and developed an upper respiratory infection which caused her readmission. At the same time she had two severe attacks of tachycardia, her pulse rising to 130-140. She has since been discharged quite fit and her pulse steady. She has been continuing with thiouracil. It is hoped to report on this case again later.—G. S.

Calcinosis Universalis.—A. P. NORMAN, M.B. (for DONALD PATERSON, F.R.C.P.).

G. H., female, aged 3½ years.

Normal birth; milestones passed normally. Brother and sister alive and well.

At the age of 17 months the child stopped crawling and objected to her limbs being moved; since then she has made no attempt to move about, but will support herself if sat up. At the age of 2 years she developed abscesses on the buttocks; a few months later hard lumps were noticed in the skin around the lower ribs.

Examination on 29.5.46 showed a small child, not thin, the face pink with a violet tinge, especially round the eyes, the skin smooth and glossy. No visceral or neurological abnormality found. Scars of healed abscesses on buttocks. Wasting of buttocks and legs. Limitation of movement at hip, knee and ankle, any attempt at movement causing great distress. Hard nodules about the size of a pea were present deep to the skin of upper thighs and lower ribs, mostly posteriorly. Recent examinations show slight improvement in joint movement.

Radiological findings (3.6.46).—Widespread deposit of calcium in soft tissues; calcium content of bones possibly diminished.

Biochemistry.—Serum calcium 9·5 mg. per 100 c.c. Alkaline plasma phosphatase 8·4 units. Inorganic blood phosphorus 4·1 mg. per 100 c.c. Blood cholesterol 136 mg. per 100 c.c. B.S.R. 39 mm. in one hour.

Blood-count.—R.B.C. 4,500,000; Hb. 95% (13·3 grammes); W.B.C. 10,000 (polys. 34%, lymphos. 64%, eosinos. 2%).

Biopsy report (Dr. Martin Bodian).—Epidermis is thin and keratinization not well marked. The corium contains a thick layer of dense collagen which does not interfere with nutritional supply of hair follicles, arrectores pilorum and sweat glands. Beneath the collagen is a layer of normal fat and beneath this are large nodules of necrotic fat cells; there is also calcification. The nodules are surrounded by fibrous tissue bands with small clusters of lymphocytes. There is hyaline degeneration of muscle with loss of cross striation and small clusters of lymphocytes are present in the intermuscular septa.

Dr. Herbert Levy drew attention to a paper by J. J. C. P. A. Rovers (*Acta. med. Scand.*, 1939, 100 57) which reported complete recovery from severe calcinosis universalis in a girl aged 5 following two courses of five weeks' treatment with sodium citrate (3 grammes daily) and occasional intravenous administration of calcium gluconate. This treatment had been suggested by Professor Snapper because of the increased ability of the plasma proteins to bind calcium when the reaction of the blood is changed in an alkaline direction. Serum calcium and inorganic phosphate rose during the treatment up to double the normal levels.

Dr. Levy had himself observed disappearance of peri-articular calcification in an adult after such treatment but spontaneous recovery occasionally occurs.

Sclerema.—A. P. NORMAN, M.B. (for DONALD PATERSON, F.R.C.P.).

G. P., male, aged 11 months. (Born 11.12.45.)

Full-term child, with normal delivery, but history of septicæmia in the mother during pregnancy. At five months the right wrist became red and swollen, and two days later the left wrist became similarly affected and later the legs became swollen and hard but not red. He had slight fever for one week and was treated with penicillin without effect.

On admission the child was apyrexial and notably happy; the skin of the face seemed pale, glazed and greyish; firm plaques were palpable under and attached to the skin on thighs, legs, feet and arms.

Radiological report (25.6.46).—Thickening of the soft tissues and coarsening, with shadows almost of the density of calcium.

Blood-count.—R.B.C. 4,600,000; Hb. 95% (13·3 grammes); W.B.C. 17,500 per c.mm. (polys. 54%, stabs 4%, lymphos. 31%, monos. 6%, eosinos. 5%).

B.S.R. 9 mm. in one hour.

Post-nasal swab.—A few colonies of coagulase-positive *Staph. aureus.*

Biopsy report (Dr. Martin Bodian).—In the corium there are clusters of large fat cells with few nuclei, surrounded by fibrous tissue and giant cells. There is evidence of calcification confirmed by von Kossa stain. A few vessels show endarteritis obliterans of various degrees. Doubly refractile crystals present within the fat cells, giving the staining reactions of neutral fat.

Congenital Syphilis.—J. HEBER, M.B., B.S. (for MARY WILMERS, M.D.).

Peter J., aged 2 months. Weight 9 lb. 15 oz.

History.—Severe snuffles and a thick purulent nasal discharge since birth. Peeling of hands and feet noticed for three weeks. Macular rash noticed two weeks ago.

Family history.—Father away in the Army in Greece. Returned home on leave for one month in December 1945 and in May 1946. No discharge, sores or rash noticed by the wife at this time. She is alive and well and never has had any symptoms. Normal pregnancy, leading to the normal delivery of a 7 lb. baby. No treatment during pregnancy. Three other children all alive and well. One miscarriage in 1943 at three months.

On examination.—A typical congenital syphilitic with severe snuffles, enlarged liver and spleen, typical rash on lower limbs and buttocks; anal fissures, maculopapular rash down the inner sides of the legs with reddened, peeling palms of hands and soles of feet. Early rhagades. No clinical epiphysitis.

Investigations.—W.R. and Kahn positive in both mother and baby. Baby's blood-count: R.B.C. 3,800,000; Hb. 68%; W.B.C. 9,000. Differential normal. X-ray of long bones: Marked periostitis. Some epiphysitis.

Treatment.—Mercury inunctions, given as an out-patient for two weeks with no improvement. Then penicillin, total dose 120,000 units per kg. body-weight, in 60 doses at four-hourly intervals, combined with daily mercury inunctions.

Progress.—After three days general condition much improved and gained weight. Rash disappeared; snuffles decreased with marked diminution of the nasal discharge, rhagades treated.

Tuberculous Abscess Formation following Penicillin Therapy.—P. J. COOPE, M.B. (for J. C. R. HINDENACH, F.R.C.S.).

C. B., male, aged 2 years 9 months.

14.9.46: Admitted with indurated swelling in left side of neck of one week's duration. Swelling incised, the pus found being sterile on culture and a few Gram-positive cocci seen on direct smear. Penicillin in saline afterwards given by injection into muscles of buttocks and thighs. Total 800,000 units. Wound healed and child discharged on eleventh day.

29.9.46: Readmitted with abscesses in the left thigh and groin and right buttock, those in thigh and buttock appearing to be deeply situated. Pus from all three abscesses contained tubercle bacilli and was sterile on culture. General condition of child good. Temperature range 97° to 100°. Abscesses are showing a tendency to reform and have been aspirated again.

Other investigations.—X-rays: No lesion in chest or spine. Tuberculin jelly test: strongly positive on 4.11.46. Blood-count: Slight hypochromic anæmia. White count and differential normal. E.S.R.: 11 mm. in one hour on 8.11.46; 18 mm. in one hour on 21.11.46.

One previous case has been reported by Ebrill and Eleck. A boy developed a tuberculous abscess in the thigh four months after a continuous intramuscular injection of penicillin in that site. The original infection for which the penicillin was given was a staphylococcal axillary abscess. It was considered by these workers that, as they could find no primary lesions in the boy, the infection was caused by the introduction of tubercle bacilli at the time of the penicillin injection. Hounslow considered that this abscess occurred as the result of a hæmatogenous spread from some primary focus elsewhere, and a hæmatoma at the site of infection forming a nidus of lowered resistance for the tubercle bacilli.

In the case presented here the fact that abscesses were present in both thighs suggests a hæmatogenous mode of infection. It is assumed that the one in the left groin was due to lymphadenitis draining that in the left thigh. It is a possibility, though unproven, that the original cervical abscess was tuberculous, as the pus was sterile. The alternative hypothesis regarding the mode of infection, also unproven, would, of course, be via contaminated syringes or needles. A special 1 c.c. syringe is kept for penicillin injections and is not used for aspirations.

Juvenile Cirrhosis.—URSULA JAMES, M.B., M.R.C.P.

Shirley G., aged 7 years 8 months.

Attended Victoria Hospital for Children as out-patient on 1.10.45, then aged 6½ years. Sent by private doctor for advice about tonsils. Backward in walking and talking (2 years+); had been taking thyroid extract ½ grain daily for four years when first seen. In 1945 normal standard at school, but spiteful, sharp-tempered and destructive. Weight 4 st. 3 lb. Tonsils large, infected. Stance round shouldered. Liver and spleen palpable and enlarged.

Family history.—One younger sibling normal. Some relatives on father's side stated to be dark skinned. Otherwise nothing relevant.

Past personal history.—Her mother had normal pregnancy and delivery. No neonatal jaundice. Pertussis, measles, mumps, bronchitis. No blood transfusions.

First admission 24.11.45.

On examination.—Dark skinned, adenoid facies, high arched palate, mouth breather. Liver firm, palpable two fingerbreadths below costal margin. Spleen firm, enlarged to umbilicus. Feet—polydactyly.

Investigations.—R.B.C. 4·2 millions. No primitive cells. Hb. 96%. W.B.C. 3,000 (polys. 69%, lymphos. 23%). Urine normal. Wassermann reaction negative. Sternal puncture: normoblastic marrow. No Gaucher's cells. Increased numbers megakaryocytes.

Discharged undiagnosed 23.12.45. Thyroid ½ grain daily continued.

Readmitted 18.2.46: Tonsillectomy and adenoidectomy. Uneventful convalescence. Discharged 8.3.46. Attended as out-patient monthly until the next admission.

April 1946: Weight 4 st. 10 lb. Spontaneous bruising of limbs noticed.

June: Liver and spleen i.s.q. Van den Bergh negative direct. Serum bilirubin 1·4 mg.% Serum proteins 8 grammes%. R.B.C. 3·7 millions; Hb. 72%; W.B.C. 4,800 (polys. 49%, lymphos. 37%, monos. 11%).

July: Red cell fragility—hæmolysis commenced 4·5% NaCl, complete at 3% NaCl. Systolic apical murmur. Hot and sweating. Emotional, with "tantrums". Thyroid stopped 22.7.46. Iron by mouth started.

August: Weight 5 st. 1¾ lb. (rapid gain since stopping thyroid). Diet—carbohydrate restriction—commenced.

September: Weight 4 st. 12 lb. Exophthalmos, fine tremor of hands, von Graefe's sign noted. Pulse 92. Otherwise physical signs unchanged. R.B.C. 4·1 millions;

Hb. 80%; W.B.C. 6,400 (polys. 70%, lymphos. 25%, monos. 5%). Blood cholesterol 276 mg.%. Mother and child Rh positive. No Rh antibody in the maternal serum. B.S.R. 10 mm. in one hour (micro-method). X-ray skull and long bones normal.

October: Weight 4 st. 12 lb. Previous physical signs unaltered except thyroid gland noted to be easily palpable. Blood sugar curve: Fasting 93 mg.%. 115 mg.% after 2½ hours. Maximum rise 133 mg.%. No glycosuria. Platelet count normal.

Readmitted 28.10.46: R.B.C. 4·3 millions; Hb. 82%; W.B.C. 6,000 (polys. 51%, lymphos. 43%, monos. 6%). Sternal puncture—Gaucher's cells absent. Normal marrow picture. Biopsy of skin—intense melanin deposit in basal layers, no hæmosiderin. Blood: Cholesterol 258 mg.%. Thymol turbidity 3 units. Alkaline phosphatase 49 units. Serum bilirubin 1·2 mg.%. Van den Bergh delayed, weakly positive.

November 26: Laparotomy. Spleen smooth, very vascular, enlarged to umbilicus. Liver small, rounded margin, hard. Liver section for biopsy. Uneventful convalescence. Discharged home 8.12.46.

Biopsy of liver (Dr. J. D. Gray).—The architecture of the liver has altered: the lobular pattern replaced by strands of fibrous tissue spreading out from the portal spaces cutting the lobules into an irregular pattern. The bile ducts are dilated and here and there small ducts unrelated to the portal spaces can be seen lying in the fibrous tissue strands. In other peri-portal areas are collections of lymphocytes, polymorphs and fibroblasts. In the liver parenchyma the bile canaliculi are dilated; thrombi were not seen. The liver cells are not remarkable.

Discussion on pathological findings.—From the biochemical point of view the persistently high blood cholesterol, high blood alkaline phosphatase and moderately increased plasma bilirubin were suggestive of a liver lesion of the obstructive type. More evidence was obtained when the abnormal blood sugar curve was fitted into the pattern—for it indicated the probability of liver parenchymal destruction. When these facts were related to the clinical observations a cirrhotic liver appeared to be the most likely consideration. The presence of a normal thymol turbidity test was not unexpected as the plasma protein estimation had shown no pathological variation. The histological picture was therefore in complete keeping with the biochemical findings.

The recent work of Dible *et al.* on the relationship between infective hepatitis and cirrhosis should be borne in mind when considering multilobular cirrhosis—as exhibited by the histological picture this case presents. A preceding zonal and focal necrosis with the necrotic parenchymal tissue replaced by the proliferating ducts and their attendant fibroblasts could be visualized when studying the sections.

A diagnosis of multilobular cirrhosis of the liver with congestive spleen has been made in this case, but the label does not embrace the mental retardation, the thyroid changes with a transient hyperthyroidism and the excessive weight. The ætiology of the cirrhosis is not known; there is no previous history of any illness that might predispose to its development.

Hepatosplenomegaly: For Diagnosis.—C. F. SAUNDERS, L.R.C.P., M.R.C.S. (for PHILIP EVANS, F.R.C.P.).

Male, aged 4 years 10 months. Only child. Birth weight 6 lb. 13 oz. Did not gain well in infancy. At age 7 months to 10 months he was in hospital with measles and whooping cough. Weight 10 lb. at age of 10 months. Frequent colds since then and has remained thin, but otherwise well.

On examination.—6.11.46: Liver enlarged two fingerbreadths, sharp edge. Spleen enlarged ½ inch below umbilicus, smooth, not tender.

27.11.46: Generalized glandular enlargement. Glands discrete, not tender. Temperature 101°. The spleen now reaches to the left pubic ramus.

Investigations.—Blood-count: R.B.C. 4,880,000; Hb. 84%; C.I. 0·87; W.B.C.

6,400 (polys. 56%, lymphos. 43%, monos. 1%). Fragility of R.B.C.: No hæmolysis in 0·46% NaCl. Serum cholesterol 174 mg. per 100 ml. W.R. negative. Tuberculin jelly test negative. Urine normal. Lævulose tolerance test normal. Blood urea 32 mg. per 100 ml. Van den Bergh reaction: direct, negative; indirect, total bilirubin less than 0·2 mg. per 100 ml. Thymol turbidity test 5 units. Total serum proteins 6·25 gm. per 100 ml. Albumin globulin ratio in serum: 2·51 : 1. Repeat blood-count (30.11.46): R.B.C. 3,000,000; Hb. 56%; W.B.C. 7,000 (polys. 36%, lymphos. 64%).

Intracranial Hæmangioma Causing Convulsions.—M. W. WEST, M.B. (introduced by R. C. LIGHTWOOD, M.D.).

Kenneth M., aged 9 years.

17.10.46: Admitted to hospital. Had suffered from convulsions for the past eighteen months, increasing in frequency.

History.—Full-term child, birth weight 5½ lb. Difficult breech delivery, forceps employed. Was not expected to live; cyanosed for three weeks and did not cry normally for a month. However, development was normal, child was in fact somewhat "forward". Sat up at 7 months, walked at 12 months and talked at 18 months. Left internal strabismus noticed at age 2 weeks. Two operations for this. Measles at 3 years.

History of present condition.—First convulsion eighteen months ago. Since then convulsions have occurred monthly until six months ago, since when three-weekly, fortnightly and finally three or four times a week. None for three weeks until child had one shortly before admission (13.10.46). Convulsions are nocturnal and are preceded by a cry. Right arm and leg twitch, there is frothing at the mouth and the head jerks towards the right. This clonic stage lasts fifteen to twenty minutes and is followed by flaccidity lasting five to ten minutes before motor power returns. No incontinence during convulsions but patient occasionally vomits. Has never had sedatives.

On examination.—Intelligent normal child. No abnormal physical signs beyond tendency to left internal deviation.

Investigations.—X-ray skull: Oval area of very thin bone to right of internal occipital protuberance. Prominent vascular channel taking origin in two groups of diploic veins and running across R. parietal bone. Slight asymmetry of vault. Volume of L. hemicranium greater than R. Air encephalogram gave no additional information. Radiologist's opinion that appearances were suggestive of intracranial hæmangioma and that there was likelihood of additional information being obtained by arteriography did not justify the risks of such procedure. E.E.G.: Repeated bursts of atypical "spike and dome" waves L. hemisphere, seen diffusely but mostly in cerebral area. No single focal area: Suggests diffuse, probably atrophic lesion, L. hemisphere. It was proposed to treat this case by X-radiation.

Angioma of the Basal Ganglia.—L. J. ROWLEY, M.B. (for DONALD PATERSON, F.R.C.P., and WYLIE MCKISSOCK, O.B.E., M.S.).

P. C., boy aged 9 years.

Attended Out-Patients' Department with a history of the onset of a limp four years ago. Six weeks ago was noticed to be using his left hand more than his right. He also had weakness of the right side of his face which his mother said had been present all his life.

Abnormal physical signs.—Bruit best heard over the left eyeball and left side of the head. Nævus, a very faint "port wine stain" above the left eye. Fundi: Right is normal, left shows tortuosity and dilatation of the veins, but no hæmangiomatous formation. Hemiparesis on the right side: (1) Upper motor type of facial paresis; (2) weakness, wasting and hypotonicity, more marked in the arm than in the leg;

(3) plantar responses, Rt. extensor, Lt. flexor. Eye movements: (1) Limitation of elevation; (2) inability to converge.

Investigations.—X-rays of skull show no abnormality. Ventriculogram shows displacement of the lower and anterior part of the third ventricle to the right. This indicates an expanding lesion in the left caudate nucleus. Angiography: Antero-posterior and lateral views show a large angioma of the left basal ganglia.

Treatment.—Deep X-ray therapy. Dose 2,250 r units.

Result.—No improvement one week after completing the course of treatment.

Staphylococcal Pneumonia with Obstructive Emphysema.—L. G. SCOTT, M.B., B.S. (for DONALD PATERSON, F.R.C.P.).

D. S., male. Admitted 28.8.46, aged 3 weeks.

History.—A small spot appeared on his chin one week previously which became septic. Two or three more septic spots appeared on the chin and a submandibular abscess was opened one day before admission. A slight cough and grunting respirations were present for three days before admission.

On examination.—Temperature 102°; pulse 122; respirations 59. Not cyanosed. Impaired percussion note over the right side anteriorly and in the right upper zone posteriorly. Râles all over the right side of the chest. The submandibular abscess was discharging and the umbilicus was sticky.

Investigations.—Blood culture and swabs from throat, umbilicus and boil grew coagulase-positive *Staph. aureus.* X-ray of chest: collapse and consolidation in the right upper lobe. W.B.C. 35,500 per c.mm. (polys. 71%, lymphos. 29%).

Progress.—Baby became very ill and cyanosed, and X-ray on 3.9.46 showed clearing in the right upper lobe and an opacity in the right lower lobe. The general condition then improved and on 9.9.46 X-ray showed a cystic appearance at the right base. The mediastinum subsequently became greatly displaced towards the left side by the obstructive emphysematous condition on the right side. The chest was needled on 19.9.46 in the fifth space in the mid-axillary line on the right side and about 15 to 20 c.c. of air removed which did not appear to be under great pressure. There was slight relief of the mediastinal displacement. About this time the baby's condition again deteriorated and he had very loose stools. He eventually improved and on 9.10.46 X-ray showed the mediastinum to be approximately central although there was still a cystic appearance on the right side. Discharged on 14.10.46, gaining weight slowly (weight 7½ lb.).

He was last seen as an out-patient on 11.11.46 and he had then gained 2 lb. 3 oz. in weight since discharge. X-ray of his chest showed some collapse in the right upper lobe. The case is being kept under observation.

Treatment.—Penicillin 3,000 units four-hourly intramuscularly (total of 585,000 units). A course of sulphathiazole (3·75 grammes) and later of sulphadiazine (total 6 grammes) was given. The baby was nursed in an oxygen tent for about one month and a penicillin spray was given in this for forty-eight hours on 11 to 13.9.46. A blood transfusion of 120 c.c. was given on 14.9.46 (R.B.C. 3,900,000 per c.mm. two days previously).

Spontaneous Bilateral Pneumothorax Occurring in a Premature Baby During the Neo-Natal Period.—JEAN W. PAUL, M.B. (for S. YUDKIN, M.R.C.P.).

R. S., male, aged 16 days, was admitted on October 4, 1946, with a history of a convulsive attack occurring half an hour after the 6 p.m. feed on that day. No previous similar attacks had been noticed by the mother.

The birth had occurred thirty-eight days prematurely following a second mild antepartum hæmorrhage. The delivery had been normal and the birth weight was 4 lb. 10 oz. Jaundice and cyanosis had been noticed during the first few days and the child had some difficulty in sucking. After discharge from the Maternity

6,400 (polys. 56%, lymphos. 43%, monos. 1%). Fragility of R.B.C.: No hæmolysis in 0·46% NaCl. Serum cholesterol 174 mg. per 100 ml. W.R. negative. Tuberculin jelly test negative. Urine normal. Lævulose tolerance test normal. Blood urea 32 mg. per 100 ml. Van den Bergh reaction: direct, negative; indirect, total bilirubin less than 0·2 mg. per 100 ml. Thymol turbidity test 5 units. Total serum proteins 6·25 gm. per 100 ml. Albumin globulin ratio in serum: 2·51:1. Repeat blood-count (30.11.46): R.B.C. 3,000,000; Hb. 56%; W.B.C. 7,000 (polys. 36%, lymphos. 64%).

Intracranial Hæmangioma Causing Convulsions.—M. W. West, M.B. (introduced by R. C. Lightwood, M.D.).

Kenneth M., aged 9 years.

17.10.46: Admitted to hospital. Had suffered from convulsions for the past eighteen months, increasing in frequency.

History.—Full-term child, birth weight 5½ lb. Difficult breech delivery, forceps employed. Was not expected to live; cyanosed for three weeks and did not cry normally for a month. However, development was normal, child was in fact somewhat "forward". Sat up at 7 months, walked at 12 months and talked at 18 months. Left internal strabismus noticed at age 2 weeks. Two operations for this. Measles at 3 years.

History of present condition.—First convulsion eighteen months ago. Since then convulsions have occurred monthly until six months ago, since when three-weekly, fortnightly and finally three or four times a week. None for three weeks until child had one shortly before admission (13.10.46). Convulsions are nocturnal and are preceded by a cry. Right arm and leg twitch, there is frothing at the mouth and the head jerks towards the right. This clonic stage lasts fifteen to twenty minutes and is followed by flaccidity lasting five to ten minutes before motor power returns. No incontinence during convulsions but patient occasionally vomits. Has never had sedatives.

On examination.—Intelligent normal child. No abnormal physical signs beyond tendency to left internal deviation.

Investigations.—X-ray skull: Oval area of very thin bone to right of internal occipital protuberance. Prominent vascular channel taking origin in two groups of diploic veins and running across R. parietal bone. Slight asymmetry of vault. Volume of L. hemicranium greater than R. Air encephalogram gave no additional information. Radiologist's opinion that appearances were suggestive of intracranial hæmangioma and that there was likelihood of additional information being obtained by arteriography did not justify the risks of such procedure. E.E.G.: Repeated bursts of atypical "spike and dome" waves L. hemisphere, seen diffusely but mostly in cerebral area. No single focal area: Suggests diffuse, probably atrophic lesion, L. hemisphere. It was proposed to treat this case by X-radiation.

Angioma of the Basal Ganglia.—L. J. Rowley, M.B. (for Donald Paterson, F.R.C.P., and Wylie McKissock, O.B.E., M.S.).

P. C., boy aged 9 years.

Attended Out-Patients' Department with a history of the onset of a limp four years ago. Six weeks ago was noticed to be using his left hand more than his right. He also had weakness of the right side of his face which his mother said had been present all his life.

Abnormal physical signs.—Bruit best heard over the left eyeball and left side of the head. Nævus, a very faint "port wine stain" above the left eye. Fundi: Right is normal, left shows tortuosity and dilatation of the veins, but no hæmangiomatous formation. Hemiparesis on the right side: (1) Upper motor type of facial paresis; (2) weakness, wasting and hypotonicity, more marked in the arm than in the leg;

Section of Anæsthetics

President—Stanley Rowbotham, M.D.

[*December* 6, 1946]

DISCUSSION: SHOCK WITH SPECIAL REFERENCE TO ANÆSTHESIA

Professor H. N. Green: It is with some hesitation that I discuss the relationship between anæsthesia and shock because, whilst we know the exciting factors and some of the manifold reactions in these two general states, we know little of the fundamental mechanisms involved in either. To interrelate two unknown mechanisms is impossible and any attempt must therefore be purely speculative. Unfortunately speculation and dogma are the highlights of innumerable discussions on shock. However, comparable experimental data concerning the part that anæsthetics play in the induction of or prevention of shock are so few that we must perforce in some degree guess how the two conditions may react on each other. It must from the start be emphasized that we are guessing and by doing so emphasizing the need for more refined experimental observation.

Among the most important questions requiring answers are the following:

(1) Are general anæsthesia and shock completely different or completely similar states, or have they merely certain common features? Are therefore their effects independent or reinforcing, or are they even antagonistic?

Less theoretical questions, though intimately linked with the first are:

(2) Does the dose of anæsthetic required vary inversely with the degree of shock and if so what is the quantitative relationship?

(3) What anæsthetic, or combination of anæsthetics, least favours the induction of shock by tissue injury and is this same anæsthesia necessarily best in established shock?

(4) Does, in fact, shock still remain an important problem for the anæsthetist or has modern anæsthesia so developed that it has automatically established the conditions least damaging to the tissues and therefore to the promotion of shock?

To none of these questions is there a complete answer but all are germane to the topic and I will speculate briefly on some of the points raised, in the hope that discussion may be provoked.

Between general anæsthesia and shock there are superficial resemblances, for the severely shocked patient is well on the way to unconsciousness and in both conditions there is a general depression of all vital activities. The blood-pressure falls, the respirations become slow and shallow, there is profound muscular relaxation and the body temperature is low. In anæsthesia the higher nervous centres are more profoundly affected than in shock but in the advanced stages of shock loss of consciousness, as evidenced by absence of response to painful stimuli and diminu-

Hospital he had been breast-fed satisfactorily without any apparent cyanosis or difficulty in sucking.

It was the ninth pregnancy. There had been no previous premature births or miscarriages, all previous deliveries had been normal, and no congenital defects had been noted in any of the family. Both parents are in good health.

On admission to the Casualty Department, soon after the convulsion, the baby was very collapsed and pale, but no cyanosis or respiratory difficulty was noted. The baby made a quick recovery, and subsequently nothing abnormal was noted on physical examination, and there were no abnormal physical signs in the lungs.

A provisional diagnosis of a cerebral attack associated with prematurity was made, but a routine X-ray of chest on the following day showed a bilateral pneumothorax. Four days later X-ray showed re-expansion of the left lung.

The baby was discharged from hospital on October 9. X-ray on the 17th showed no change, but by November 2 complete re-expansion had taken place.

Thus complete resolution of the condition occurred within twenty-eight days of the diagnosis having been made, and at no time had there been any physical signs or symptoms of a pneumothorax.

The majority of reported cases of pneumothorax in the newborn have been associated with difficult births, asphyxia, or attempts at artificial respiration. These cases have usually shown definite evidence of the condition and have been called spontaneous *pneumothorax abrupta*. A second group of cases in which symptoms have developed gradually have been termed spontaneous *pneumothorax lenta* and infective processes and congenital lung defects have been included in the ætiology.

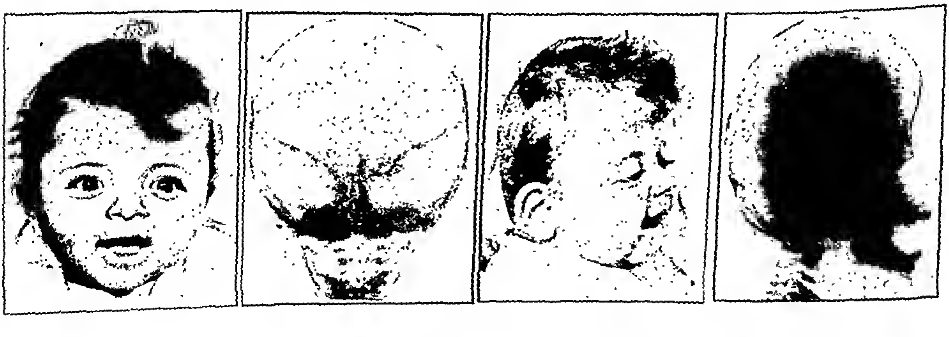
In 1940 De Costa (*Amer. J. Obstet. Gynec.*, **39**, 378) put forward the view that the condition may occur more commonly than is generally recognized; and in 1930 a routine radiographic review of 702 newborn babies (Davies and Stevens, *Amer. J. Obstet. Gynec.*, **20**, 73) included six cases of symptomless pneumothorax.

This case seems to fall into this third class of symptomless pneumothorax, which would have remained undiagnosed in the absence of a routine X-ray.

It was suggested that the pneumothorax might have occurred during the convulsive attack; but in view of the occasional cyanosis noted in the first few days after birth, it was felt that the possibility of a long-standing pneumothorax dating from birth could not be excluded.

Oxycephaly.—PHILIP EVANS, M.D.

Boy aged 7 months. Mother and father healthy, not consanguineous. Pregnancy and labour normal. Head of baby noticed to be abnormal in shape at birth.



Oxycephaly. Infant aged 7 months.

On examination.—Child healthy, weight 18½ lb., head circumference 16¼ in. Typical appearance of oxycephaly without exophthalmos. Anterior fontanelle admits finger tip; metopic suture not felt, other suture lines palpable.

The child is bright, cheerful and without obvious visual disturbance.

hæmorrhagic shock (Bennett *et al.*, 1944) and the work of the M.R.C. Committee (1918) on acidosis and shock showed how easily ether in excessive amounts would precipitate shock in artificially induced acidosis in the cat. The possibility of overdosage is, however, always to the fore. For instance, Lorbor *et al.* (1940) claimed in opposition to O'Shaughnessy and Slome (1935), that deep anæsthesia in cats favoured the onset of traumatic shock, for under ether *analgesia* the animal was more resistant to shock than under chloralose or nembutal anæsthesia. The interpretation of all experimental work on shock is complicated by the extra factor of anæsthesia and unfortunately, as in clinical work, the choice of anæsthetic often depends on the anæsthetist being experienced in one type of anæsthesia. For this reason there is not much guide in the literature to the relative merits of different anæsthetics in either potential or established shock. The observations of Bennett *et al.* (1944) are the best recent approach to this problem. They compared the effects of sodium evipan, ether and cyclopropane on the circulation of dogs before and after the induction of hæmorrhagic shock. They conclude that cyclopropane offers the best margin of safety with respect to blood-pressure and blood flow through essential vascular beds. It is impossible to compare the normal and anæsthetized animal but it should be possible to compare a wide range of anæsthetics at the same degree of anæsthesia. Now that more standardized methods of shock induction, particularly that of limb ischæmia in rodents, have been evolved such an arduous investigation could now be undertaken. Only thus might the precise information, which we now completely lack, be obtained.

My own experience provides but little practical help in the problem but does not suggest that all anæsthetics necessarily lower the tolerance to shock-inducing methods. For instance neither light ether nor anæsthetic doses of the barbiturate nembutal, significantly increase the susceptibility of rats to adenosine triphosphate shock and there are indications that ether analgesia may decrease it. Here I must digress to explain this method of shock induction and a curious relationship of an unusual anæsthetic to it.

I have shown (Green, 1943) that pure adenosine triphosphate obtained from muscle (Bielschowsky and Green, 1943) is capable of producing a shock-like state when injected into a wide variety of animals. This substance has a wide distribution in the body and is of great physiological importance, for by the high energy potential of its terminal phosphate bond it provides the energy for muscular contraction and no doubt for many other energy transformations in the body. Now in the presence of a raised tissue magnesium content the effective dose of adenosine triphosphate is strikingly reduced (Green and Stoner, 1944). Moreover, under similar conditions the shock-inducing action of tissue injury is enhanced or accelerated. Here then is a substance, magnesium, with anæsthetic properties which increases the susceptibility of the organism to shock-inducing stimuli. Or the result may be interpreted as that of a shock-inducing agent increasing the susceptibility to an anæsthetic. A correct interpretation is not so simple as it might appear because magnesium anæsthesia and fully developed adenosine triphosphate shock are, superficially at least, strikingly similar. These findings have obviously some importance in relation to the mechanism of shock and possibly to the rôle which adenosine triphosphate undoubtedly plays in it. They have, however, no immediate relevance to the relation between anæsthesia and shock for no such potentiation of adenosine triphosphate is brought about by ether or nembutal. It may be noted, however, that as this form of shock develops, the effective dose of anæsthetics, as with shock however induced, is progressively reduced, until a point is reached at which shock from a practical standpoint is itself anæsthesia.

It was the observation of the anæsthetic state seen in advanced adenosine triphosphate shock which led me to consider a possible relationship between the two tion or absence of the corneal reflex may be observed in an animal which still retains the power of recovery. Such observations are made more readily in the experimental animal and indeed there may be no obvious difference between the appearance of an animal in deep shock and in deep anæsthesia.

Apparent similarities are to be found when we probe somewhat deeper. The oxygen consumption of the body (McClure *et al.*, 1939) and of individual tissues (Quastel, 1932) falls in response to anæsthetics and this fact is one of the most prominent features of the shock state as Aub (1920) first clearly demonstrated in cats following trauma to the hind limbs. Though the reported blood volume changes in general anæsthesia are variable with some anæsthetics, particularly ether, hæmoconcentration and a fall in volume have been recorded (Boycott and Price-Jones, 1922; Stewart and Rourke, 1938). Are these similarities merely fortuitous or do they indicate some more fundamental connexion between the two states? We do not know but there are some practical and theoretical considerations which suggest that the possibility of some common factor in the mechanism of shock and anæsthesia might be further explored.

In established shock I imagine that no anæsthetist would dispute the statement, and it is certainly my experience in experimental shock, that the amount of anæsthetic required to produce full anæsthesia is very much reduced and varies inversely with the degree of shock. More exact quantitative data are, however, required, particularly as I am sure the figures would be impressive enough to make no one, even the most inexperienced, question the ever-present danger of overdosage in established shock. On the question of whether anæsthetics render the animal more sensitive to shock-inducing agents, we are not on such firm ground. Clinical observations in the 1914-18 war by Marshall (1917) and Cannon (1923) suggested that ether and chloroform anæsthesia, as judged by their effect on blood-pressure and post-operative complications could be highly dangerous in the severely injured though not necessarily clinically shocked man. Later laboratory investigations indicated that their effect on blood-pressure was mainly due to a depressant action on heart muscle. Nitrous oxide, with efficient oxygenation, had not this effect and these observers found this by far the most satisfactory anæsthetic for battle casualties. Their observations were given apparently strong support by the observation of Dale (1919) that the etherized cat was far more susceptible to the shock-inducing action of histamine than was the unanæsthetized or nitrous oxide and oxygen anæsthetized animal. The obvious difficulty in interpreting such results is that two different levels of anæsthesia were being compared and moreover the ether anæsthesia could well have been so deep as to complicate the experiment by adding the effects of tissue anoxia and overdosage. Since it is now known that histamine is not responsible for traumatic shock the observations are not so pertinent to the clinical problem as at one time appeared.

There is, of course, no doubt that, anæsthetics, being potentially toxic agents, can, at some concentration within the recoverable range produce tissue damage, or that an associated tissue anoxia will produce additional damage. But, and here I am open to correction, there is no absolute proof that every type of anæsthesia must necessarily produce these secondary effects in any significant degree. There are, of course, plenty of experimental and clinical observations suggesting that some general anæsthetics do make the organism more susceptible to shock. Chloroform in particular has long been suspect both in the clinics and laboratory, and in experimental work chloralose has a bad reputation (Freedman and Kabat, 1940). In fact, Blalock and Cressman (1939) suggested that good results with spinal anæsthesia in traumatic shock (O'Shaughnessy and Slome, 1935) might have been due to a protective action against the convulsive effect of chloralose. Even ether has been reported to increase the susceptibility of cats to traumatic shock (Kabat, 1940) and dogs to hæmorrhagic shock (Bennett *et al.*, 1944) and the work of the M.R.C. Committee (1918) on acidosis and shock showed how easily ether in excessive amounts would precipitate shock in artificially induced acidosis in the cat. The possibility of overdosage is, however, always to the fore. For instance, Lorbor *et al.* (1940) claimed in opposition to O'Shaughnessy and Slome (1935), that deep anæsthesia in cats favoured the onset of traumatic shock, for under ether *analgesia* the animal was more resistant to shock than under chloralose or nembutal anæsthesia. The interpretation of all experimental work on shock is complicated by the extra factor of anæsthesia and unfortunately, as in clinical work, the choice of anæsthetic often depends on the anæsthetist being experienced in one type of anæsthesia. For this reason there is not much guide in the literature to the relative merits of different anæsthetics in either potential or established shock. The observations of Bennett *et al.* (1944) are the best recent approach to this problem. They compared the effects of sodium evipan, ether and cyclopropane on the circulation of dogs before and after the induction of hæmorrhagic shock. They conclude that cyclopropane offers the best margin of safety with respect to blood-pressure and blood flow through essential vascular beds. It is impossible to compare the normal and anæsthetized animal but it should be possible to compare a wide range of anæsthetics at the same degree of anæsthesia. Now that more standardized methods of shock induction, particularly that of limb ischæmia in rodents, have been evolved such an arduous investigation could now be undertaken. Only thus might the precise information, which we now completely lack, be obtained.

My own experience provides but little practical help in the problem but does not suggest that all anæsthetics necessarily lower the tolerance to shock-inducing methods. For instance neither light ether nor anæsthetic doses of the barbiturate nembutal, significantly increase the susceptibility of rats to adenosine triphosphate shock and there are indications that ether analgesia may decrease it. Here I must digress to explain this method of shock induction and a curious relationship of an unusual anæsthetic to it.

I have shown (Green, 1943) that pure adenosine triphosphate obtained from muscle (Bielschowsky and Green, 1943) is capable of producing a shock-like state when injected into a wide variety of animals. This substance has a wide distribution in the body and is of great physiological importance, for by the high energy potential of its terminal phosphate bond it provides the energy for muscular contraction and no doubt for many other energy transformations in the body. Now, in the presence of a raised tissue magnesium content the effective dose of adenosine triphosphate is strikingly reduced (Green and Stoner, 1944). Moreover, under similar conditions the shock-inducing action of tissue injury is enhanced or accelerated. Here then is a substance, magnesium, with anæsthetic properties which increases the susceptibility of the organism to shock-inducing stimuli. Or the result may be interpreted as that of a shock-inducing agent increasing the susceptibility to an anæsthetic. A correct interpretation is not so simple as it might appear because magnesium anæsthesia and fully developed adenosine triphosphate shock are, superficially at least, strikingly similar. These findings have obviously some importance in relation to the mechanism of shock and possibly to the rôle which adenosine triphosphate undoubtedly plays in it. They have, however, no immediate relevance to the relation between anæsthesia and shock for no such potentiation of adenosine triphosphate is brought about by ether or nembutal. It may be noted, however, that as this form of shock develops, the effective dose of anæsthetics, as with shock however induced, is progressively reduced, until a point is reached at which shock from a practical standpoint is itself anæsthesia.

It was the observation of the anæsthetic state seen in advanced adenosine triphosphate shock which led me to consider a possible relationship between the two tion or absence of the corneal reflex may be observed in an animal which still retains the power of recovery. Such observations are made more readily in the experimental animal and indeed there may be no obvious difference between the appearance of an animal in deep shock and in deep anæsthesia.

Apparent similarities are to be found when we probe somewhat deeper. The oxygen consumption of the body (McClure *et al.*, 1939) and of individual tissues (Quastel, 1932) falls in response to anæsthetics and this fact is one of the most prominent features of the shock state as Aub (1920) first clearly demonstrated in cats following trauma to the hind limbs. Though the reported blood volume changes in general anæsthesia are variable with some anæsthetics, particularly ether, hæmoconcentration and a fall in volume have been recorded (Boycott and Price-Jones, 1922; Stewart and Rourke, 1938). Are these similarities merely fortuitous or do they indicate some more fundamental connexion between the two states? We do not know but there are some practical and theoretical considerations which suggest that the possibility of some common factor in the mechanism of shock and anæsthesia might be further explored.

In established shock I imagine that no anæsthetist would dispute the statement, and it is certainly my experience in experimental shock, that the amount of anæsthetic required to produce full anæsthesia is very much reduced and varies inversely with the degree of shock. More exact quantitative data are, however, required, particularly as I am sure the figures would be impressive enough to make no one, even the most inexperienced, question the ever-present danger of overdosage in established shock. On the question of whether anæsthetics render the animal more sensitive to shock-inducing agents, we are not on such firm ground. Clinical observations in the 1914-18 war by Marshall (1917) and Cannon (1923) suggested that ether and chloroform anæsthesia, as judged by their effect on blood-pressure and post-operative complications could be highly dangerous in the severely injured though not necessarily clinically shocked man. Later laboratory investigations indicated that their effect on blood-pressure was mainly due to a depressant action on heart muscle. Nitrous oxide, with efficient oxygenation, had not this effect and these observers found this by far the most satisfactory anæsthetic for battle casualties. Their observations were given apparently strong support by the observation of Dale (1919) that the etherized cat was far more susceptible to the shock-inducing action of histamine than was the unanæsthetized or nitrous oxide and oxygen anæsthetized animal. The obvious difficulty in interpreting such results is that two different levels of anæsthesia were being compared and moreover the ether anæsthesia could well have been so deep as to complicate the experiment by adding the effects of tissue anoxia and overdosage. Since it is now known that histamine is not responsible for traumatic shock the observations are not so pertinent to the clinical problem as at one time appeared.

There is, of course, no doubt that, anæsthetics, being potentially toxic agents, can, at some concentration within the recoverable range produce tissue damage, or that an associated tissue anoxia will produce additional damage. But, and here I am open to correction, there is no absolute proof that every type of anæsthesia must necessarily produce these secondary effects in any significant degree. There are, of course, plenty of experimental and clinical observations suggesting that some general anæsthetics do make the organism more susceptible to shock. Chloroform in particular has long been suspect both in the clinics and laboratory, and in experimental work chloralose has a bad reputation (Freedman and Kabat, 1940). In fact, Blalock and Cressman (1939) suggested that good results with spinal anæsthesia in traumatic shock (O'Shaughnessy and Slome, 1935) might have been due to a protective action against the convulsive effect of chloralose. Even ether has been reported to increase the susceptibility of cats to traumatic shock (Kabat, 1940) and dogs to favourable aspects of anæsthesia and shock induction. Do anæsthetics, for instance, reduce cell membrane permeability and thus restrict local fluid and electrolyte losses at the site of injury? For instance one prominent theory of anæsthetic action relates it to the redistribution in the cell membrane of surface lipoids with diminished permeability to water and water-soluble substances. On the experimental side there is the work of Pickrell (1940) who finds that anæsthetics of various kinds prevent the vascular response in infected tissues and thus presumably diminish local exudation. Slender though this evidence may be it does serve to remind us that anæsthetics may well have a therapeutic, and not merely a harmful rôle in shock.

There is another more general aspect of the problem which ought to be considered in the present context. Since I first started the study of shock in 1941 I have always expressed the view to my assistants that there is no evidence that shock is necessarily, in itself, a pathological, in the sense of harmful, state. Just as inflammation is the local reaction to injury, shock is the early general reaction, and, like inflammation, must surely be a physiological defence mechanism. There is not time here to expound this view in full. Suffice to say that every manifestation of shock has as its outcome the conservation of body energy and fluid. I have found (Green, 1945) that if this mechanism be antagonized by raising the environmental temperature above a threshold value, there is no gradual onset of shock in the injured animal but instead, after an interval in which the animal remains lively, there is sudden collapse and rapid death. The state of anæsthesia has features in common with shock, though probably not a similar mechanism. Provided therefore that the secondary toxic effects are avoided, it may well be that anæsthesia may actually be beneficial in reinforcing a general defence mechanism to injury. Even if this hypothesis were true, it would not, of course, mean that clinical shock is a desirable state any more than high fever is. Clinical shock indicates large-scale tissue injury and any increase in this by anæsthetic overdosage and anoxæmia will, of course, accentuate the general reaction, bringing it ever closer to the so-called "irreversible state" in which the energy output of the body is so low as to be incompatible with recovery. Just so, high fever may of itself produce damage to the central nervous system incompatible with life. But up to a certain point shock, like fever, must be a beneficent reaction. Unfortunately, unlike fever, we have no accurate measure of the safety limit and therefore in practice it must always be regarded as a dangerous state. Nevertheless future work may ultimately modify this view when degrees of shock can be estimated.

It will be clear, however, that we do not treat shock as such any more than we treat fever as such, but rather that we treat the offending cause. Clinical shock is the expression of large-scale tissue injury and the treatment is solely that of restoring the injured parts to normal. If the exciting cause is loss of blood and/or body fluids and electrolytes we remove the cause by giving blood. If the cause be faulty anæsthesia the treatment is not transfusion but alteration in the anæsthetic technique. In the final analysis anæsthesia is the most potent weapon in the prophylaxis of shock we have, for with it damaged tissue can be removed or restored which would often otherwise remain to kill. Not being a practical anæsthetist, it would be presumptuous of me to give advice on the least harmful mode of anæsthesia particularly as it is obvious that all developments in technique have precisely this object in view. To me it would seem that modern anæsthesia at its best has largely attained this end by refinements of technique, giving always a free airway and accurately controlled dosage. As an outsider sees it, nitrous oxide and oxygen combined, when necessary, with other methods of producing relaxation, such as curare or local anæsthesia, seem to be approaching an ideal anæsthesia wherever shock exists or may threaten.

The anæsthetist ought to become the recognized expert in clinical shock. He has the best facilities for assessing the degree of shock by the established methods states, and, as we have seen, there are undoubtedly important common features. In established shock the two states reinforce each other and it may be useful to consider some possible explanations of how the presence of shock could affect the anæsthetic dose. One theory of anæsthetic action is that the reactivity of the nerve cell is reduced by interference with intracellular oxidation. This is also a feature of shock and thus theoretically the two states might summate. This is a rather ingenuous theory but there is a more practical connexion between the general depression of shock and anæsthesia. Diminished oxidation and enzymic activity will retard the breakdown of or conversion of anæsthetics into non-narcotic substances. The diminished blood volume will increase the anæsthetic concentration of the blood and, perhaps more important still, the damped-down kidney and respiratory excretion will maintain the tissue concentration at a relatively higher level than in the normal subject. Thus, though we do not know in what way anæsthesia and shock are precisely related, the view that they are supplementary rather than complementary states seems the more plausible. Whatever view we take, however, there is no lack of sound reasons for stressing the particular importance of anæsthetic overdosage in the shocked or potentially shocked patient.

It does not follow, as I have stressed, that, because the shocked individual requires less anæsthetic, anæsthesia necessarily predisposes to shock and, in fact, it would seem that the reverse hypothesis that, in its uncomplicated form, anæsthesia is in some degree protective against shock, has points in its favour. The surgeons who first used anæsthetics were impressed, in the light of their previous experience, by the diminished degree of shock during and after major operations. The difference in a conscious patient with a wound of the gut and an anæsthetized patient undergoing a major abdominal operation is striking. We are by no means certain yet that the rôle of sensory stimuli in the induction of traumatic shock is negligible. In spite of conflicting evidence it seems fairly clear that complete section of the spinal cord does not prevent and may well be dangerous in established shock. Nor is there any convincing evidence that spinal anæsthesia has any protective action and there is little doubt that it may be dangerous after experimental shock has been induced. But the evidence is not all in the same direction and one has always felt how unlikely it was that such a profound general response to injury would be completely independent of the nervous system. The reason for some of the contradictory findings may perhaps be found in the work of Swingle and his collaborators (1944). They found that shock in dogs could be prevented by effective procaine anæsthetization of the major nerves to the traumatized limb though section of these nerves was ineffective. Complete spinal section was also ineffective. However, when the cord was only partially sectioned in such a way as to leave tracts in the ventral area intact death from an otherwise lethal injury to the limb did not occur. If this work is substantiated then the conclusion must follow that afferent nerve impulses from the injured tissue have a shock-inducing effect. It would appear that the beneficial effect of removing these impulses is nullified if at the same time other nervous connexions with the injured area are severed. My own interpretation is that the absence of efferent nervous impulses increases local fluid loss by diminishing tone in the limb vessels, for Freedman and Kabat (1940) were able to prevent traumatic shock by a combination of spinal section and limb binding. It must be concluded provisionally that afferent nerve impulses do play some part in the whole complicated genesis of shock and therefore that local and regional anæsthesia have some place in shock prophylaxis. How important a part the nervous system plays must await further investigation for most workers have hitherto appeared to assume that there was only one major exciting factor in shock, overlooking the fact that shock is not a simple state but a complex integrated mechanism set in motion by a variety of stimuli.

Even if we disregard the rôle of sensory stimuli there are other theoretically

The changes in the fit young male adult from injury, through resuscitation to operation and finally to evacuation or death, depend upon a number of factors, which No. 1 Traumatic Shock Research Team under Dr. R. T. Grant set out to investigate during the late war in Italy. As the anæsthetist of the team it fell to my lot to examine the changes at operation and to see what part anæsthesia played in their production. I wish to thank Dr. Grant for allowing me to use the findings of the team in so far as they help in the elucidation of the problems of anæsthesia. This paper is based on some 63 limb and 60 belly injuries which were mainly observed by me and constituted only a part of the total material of the team.

In limb injuries the illness of the patient depends mainly upon hæmorrhage. This is very important. Further, the clinical estimate of blood loss is often considerably less than what is found by measurement of the blood volume. A patient may appear on clinical grounds to be reasonably fit a few hours after injury and yet he has lost as much as 40% of his blood. Such a patient may have a normal blood-pressure. In general blood loss after injury depends upon the amount of damaged tissue remaining adherent to the body. If this is correlated with the clinical signs a good idea of hæmorrhage can be gained.[1]

Briefly, the signs found at operation in limb injuries depended on blood loss. The greater the blood loss after injury and the smaller the amount of preoperative transfusion the paler the face, the more the tachycardia, the lower the blood-pressure and the more intense the vasoconstriction. By this last was meant cold exposed finger tips, constricted veins, a narrow width of radial pulse and a pale skin.

In belly injuries the same was true but to a lesser extent. Tachycardia and hypotension were present in patients who had not lost much blood and had been over-transfused and who had a general peritonitis.

Other factors caused an alteration in the signs at operation. Pressor and depressor blood-pressure responses were observed in both limb and belly cases with either an increase or a slowing of the pulse-rate at the time of surgical manipulations, although these were not infrequently performed without any immediate change. Previous blood loss enhanced the depressor response. (In one case traction on the guts in the presence of a general peritonitis resulted in a sudden fall in blood-pressure and a slowing of the pulse-rate and the immediate death of the patient. Vasovagal type of response.)

Sudden blood loss at operation was associated with a depressor change with either an increase or a decrease in the pulse-rate. The greater the hæmorrhage after injury and the more rapid the loss at operation the more obvious the effects of even a small amount. (One such case with a limb injury lost ½ pint of blood suddenly. Immediately the blood-pressure fell so as to be unrecordable, there was a marked slowing of the pulse-rate (axillary), a sudden decrease in the frequency and amplitude of respirations and a dilatation of the pupils.)

In the conscious state transfusion was associated with a rise in blood-pressure and this was also observed under anæsthesia.

Anæsthesia under certain circumstances was found to alter these signs and under others to add to them. What then are the effects of anæsthesia? Are there any adverse effects and what is the significance of these?

The evidence shows that there is often a pressor effect at operation which is due to the anæsthetic. At about the end of operation when the mask or endotracheal tube is withdrawn there is frequently an abrupt fall in blood-pressure. This is due to the anæsthetic because if the mask is reapplied the pressure rises. It falls again on finally removing the mask. This test was applied in 6 cases and a positive result obtained in all. The fall in blood-pressure is independent of surgical manipulations and he is most directly concerned with the degree of tissue oxidation and for these reasons he should be concerned with wider considerations than the anæsthetic itself. He ought to be aware of the profound prophylactic effects of adequate tissue hydration, since dehydration, due to the accumulation of fluid and sodium in the injured area, is, after frank loss of blood, probably the commonest exciting cause of shock. He should know of the detrimental effect of overheating, both local and general, and the beneficial effect of local cooling of injured parts. He should be acutely aware of the much lower tolerance to shock with advancing age and in the presence of infection. Particularly should he recognize that the shock mechanism takes time to develop as a clinical entity and that the apparently good subject on the table may have his tissues so damaged by the surgeon and anæsthetist combined that the resulting death from "bronchial pneumonia" [*sic*] is really only an expression of delayed shock. In civilized man, whose injuries can usually, in some degree, be modified by active intervention, it is, at the clinically detectable stage, always undesirable. Clinical shock means extensive tissue injury and in the present state of knowledge we can take no further risks.

---

[1] For details see Report of this team when published.

REFERENCES

Aub, J. C. (1920) *Amer. J. Physiol.*, 47, 502.
Bennett, H. S., Bassett, D. L., and Beecher, H. K. (1944) *J. clin. Invest.*, 23, 181.
Bielschowsky, M., and Green, H. N. (1943) *Lancet* (ii), 153.
Blalock, A., and Cressman, R. D. (1939) *Surg. Gynec. Obstet.*, 68, 278.
Boycott, A. E., and Price-Jones, C. (1922) *J. Path. Bact.*, 25, 335.
Cannon, W. B. (1923) Traumatic Shock. New York.
Dale, H. H. (1919) Med. Res. Comm. London. Spec. Rep. Ser., No. 26.
Freedman, A. M., and Kabat, H. (1940) *Amer. J. Physiol.*, 130, 620.
Green, H. N. (1943) *Lancet* (ii), 147.
—— (1945) Not yet published.
——, and Stoner, H. B. (1944) *Brit. J. exp. Path.*, 25, 150.
Kabat, H. (1940) *Minnesota Med. Foundation Bull.*, 1, 96. Quoted Harkin, N. H. (1941) *Surgery*, 9, 447.
Lorbor, V., Kabat, H., and Welte, E. J. (1940) *Surg. Gynec. Obstet.*, 71, 469.
Marshall, G. (1917) *Proc. R. Soc. Med.*, 10, 17.
McClure, R. D., Hartman, F. W., Schnedorf, J. G., and Schelling, V. (1939) *Ann. Surg.*, 110, 835.
Medical Research Committee, London (1919) Spec. Rep. Ser., No. 26.
O'Shaughnessy, L., and Slome, D. (1935) *Brit. J. Surg.*, 22, 589.
Pickrell, K. L. (1940) *Anesth. and Analges.*, 19, 272.
Quastel, J. H. (1932) *Proc. roy. Soc. B.*, 112, 60.
Stewart, J. D., and Rourke, G. M. (1938) *J. clin. Invest.*, 17, 413.
Swingle, W. W., Kleinberg, W., Remington, J. W., Eversole, W. J., and Overman, R. R. (1944) *Amer. J. Physiol.*, 141, 54.

Dr. R. P. Harbord: Lundy has recently said in relation to "shock".

". . . the patient may have suffered an injury and may have lost blood. He may have been exposed to a strong electric current. He may have become weakened by a long and debilitating disease and may have been bedridden for a long time."

The question "what is the best anæsthetic for shock?" is thus ambiguous if by "shock" is meant a number of different conditions.

The present confusion of thought is because of this lumping together of various illnesses. When certain signs of a similar character occur, the state is dubbed "shock" irrespective of the illness or injury concerned. It is the current teaching that "shock" may develop at operation when there is a falling blood-pressure and a rising pulse-rate. When the systolic pressure reaches 80 mm.Hg and the pulse-rate 100 per minute or more clinical "shock" is said to be also present.

It is not generally realized that the combination of these signs may, under different circumstances, have all the differences in significance as between life and death. The use of a term to describe them as a syndrome is therefore misleading. A study of the responses of a standard type of patient under similar conditions yields information of a more useful kind.

scription "a good colour" although it subsequently turned out from the calculations that these patients had lost considerable amounts of blood after injury and had had little transfusion. The rapid return of facial pallor after the cessation of the administration of anæsthesia shows that the colour of the face is an unreliable sign.

Because the patient is "pink, warm and dry" at operation we should not neglect the other signs (e.g. blood-pressure and pulse-rate) or forget to consider the type of injury. When the word warm is used this should be qualified in relation to what is warm because the extremities behave differently from other parts of the body and have a different significance. Sweating may be produced by weather conditions, by ether and results from disturbances of the administration of anæsthesia.

Certain additional points in relation to the signs at operation are of importance to the anæsthetist.

(1) A hypotension may develop without any change in the facial colour or in the temperature of the extremities.

(2) Estimations of the systolic level by the feel of the radial pulse are inaccurate. (In one case the radial pulse was not palpable at the wrist and yet a manometer showed a normal blood-pressure. In this case the weather was cold and vasoconstriction was present.)

It is therefore important to use a manometer for measuring blood-pressure. This should be estimated frequently (every five minutes) in any case in whom deterioration is likely to occur.

Hypotension at operation might be due to one or more of the following:

(1) Blood loss after injury with insufficient transfusion.

(2) Further blood loss at operation.

(3) Surgical manipulation.

(4) Anæsthesia.

The significance of this sign is varied according to its cause, for example, the hypotension due to blood loss responds to transfusion although this may be insufficient to replace the loss. Hypotension due to surgical manipulation disappears after the trauma has ceased, though it may be immediately fatal as with a sudden hæmorrhage.

Hypotension due to anæsthesia was most marked in the case of chloroform. In patients with minor injuries there is no reason why a certain amount of hypotension should be harmful. It will recover when the administration ends. With injuries of a more serious character it seems unjustifiable to contribute to the hypotension. The initial pentothal produced hypotension in a few cases only. Generally in the cases having pentothal as the sole anæsthetic such hypotension as was produced could be related to causes other than anæsthesia, e.g. blood loss.

Prolonged hypotension at or after operation in a belly case with general peritonitis is a grave sign for many of these patients die soon after operation in a state of tachycardia, hypotension and vasoconstriction. Prolonged hypotension at or after operation in a limb injury is a serious sign but the patient should recover if he is adequately transfused. Transfusion should be tried in the case of the hypotension which becomes revealed after disconnecting anæsthetic apparatus because this may be due to blood loss. The use of vasoconstrictors was in some cases followed by adverse effects and they appear to be of little value in the treatment of hypotension which is due to blood loss.

It should be seldom necessary to anæsthetize a patient with a limb injury with pallor, tachycardia, hypotension and vasoconstriction because properly treated such a patient ought to reach operation with a circulation well restored.

and occurs after cyclopropane, trilene or ether. A study of the clinical details in cases in whom it was well marked shows that it was most probably due to a change in the CO_2 stimulus from rebreathing to air.

Coincidental changes were found in the facial colour which became paler, in the pulse-rate which increased, in the temperature of the extremities which cooled, and also in the respirations which became shallower.

The extent of the fall in blood-pressure was in many cases slight but in some it was sufficient to cause alarm. The fall occurred irrespective of the level of systolic blood-pressure just before the removal of the mask. The change had in several instances been preceded by a gradually progressive rise in blood-pressure. In others the pressure had been falling and this was further accentuated.

The significance of the pressor effect is as follows:

(1) The blood-pressure is maintained at a spurious level during anæsthesia.

(2) A false interpretation is obtained concerning the state of the patient. (Judgment should be made after the mask has been removed and not immediately before.)

(3) The pressor effect may reflect an additional circulatory strain.

(4) The period immediately following the removal of the mask is potentially dangerous. If the fall in systolic pressure is marked it may be wiser to defer movement or refrain from any surgical manipulation for the time being.

Other effects of anæsthesia depended upon the drug employed. The following signs were recorded in the induction period:

(1) Pentothal: A fall in blood-pressure and a rise in pulse-rate.

(2) Chloroform: A fall in blood-pressure and a slowing of the pulse-rate.

(3) Cyclopropane: A variable effect on the blood-pressure which was not marked. A fairly constant feature was the slowing of pulse-rate which occurred less frequently in those who had lost considerable amounts of blood.

(4) Ether: The effects of ether were so distorted by disturbances of the administration of anæsthesia and by the effects of other drugs used in the induction (ethyl chloride, nitrous oxide or pentothal) that it was almost impossible to observe the precise changes due to this drug. In uncomplicated cases there appeared to be but little effect.

These changes were found in both limb and belly cases. The effects of the drugs on the blood-pressure were more difficult to assess once the induction had passed because of surgical manipulations, blood loss and disturbances of the administration of anæsthesia. There was a general tendency which was more marked in the limb cases for the blood-pressure to decline progressively through operation. In spite of this tendency certain cases showed that ether anæsthesia could be prolonged for as long as two hours without the production of a hypotension.

With pentothal anæsthesia in the limb injuries there was but little alteration in the facial colour or in the temperature of the exposed extremities. With ether and cyclopropane, on the other hand, the face was frequently a deeper colour at operation and the extremities became warmer (sometimes hot), and the radial pulse wider, the veins dilated and sweating occurred, especially with ether. There was thus a well-marked vasodilatation. The flushing of the face was probably partly related to the constricting effect of the mask harness. At any rate the patient appeared to be relatively *unchanged* as judged by the facial colour with pentothal, whereas with ether or cyclopropane it looked as though his condition had improved. This "improvement" was more apparent than real. Since it is a change which is imposed upon the patient by anæsthesia it may in fact be an adverse effect. In some cases the face became sufficiently well coloured at operation to merit the de-

Pentothal had certain advantages in cases with limb injuries, e.g. an adequate depth of anæsthesia could be attained rapidly, disturbances of the administration were less, and there was less alteration of the signs of blood loss at operation. For belly injuries cyclopropane or ether after various methods of induction was found to be satisfactory if administered without disturbance. In some cases the combination of regional blocks and general anæsthesia appeared to be ideal.

Anæsthesia tends to alter the signs in the patient which have resulted from injury and hæmorrhage by pressor effects with vasodilatation. At times the initial response from anæsthetic drugs add to the signs already present. The alteration of the signs is less well marked in those who have lost considerable amounts of blood. If the patient has facial pallor, tachycardia, hypotension and vasoconstriction before the induction of anæsthesia it is probable that most of these signs will remain through operation though some may be slightly modified.

The final outcome; recovery or death, in limb injuries depends on blood loss and its treatment. In belly injuries it depends on blood loss in some cases but since a good many die of peritonitis the outcome rests with surgery.

The following points are worthy of stressing in relation to anæsthesia. Pay particular attention to the administration. Obtain a sufficient depth and do not hope for this with fantastically small amounts of the drug. Once the depth is attained maintain it with whatever is necessary. Induce anæsthesia with the head low and be ready to treat the patient who vomits.

Watch the signs carefully, particularly the blood-pressure. Hypotension may be a sign of considerable hæmorrhage. Its absence does not necessarily mean that all is well and its return to normal with transfusion does not mean that this has been sufficient. The signs in a patient should never be considered alone but in relation to his injuries and the possibility of blood loss or peritonitis. When referring to deterioration at operation we should state exactly what we mean.

I should like to thank Drs. Grant and Reeve for their constant encouragement; Dr. Daly for making available such equipment as I required; and Drs. George Edwards and Bernard Johnson and Lieut.-Colonel Scriven for advice and help.

Dr. R. J. Minnitt mentioned some research work on shock and anæsthesia which he had carried out in 1924-25. This formed the basis of a paper he read before the Section of Anæsthetics in 1932 (*Proc. R. Soc. Med.*, 26, 347). It showed that during open ether anæsthesia, when shock symptoms appeared, blood-pressure was low and blood sugar high. After the operation was over the blood-pressure rose again, and the blood sugar fell. He asked Dr. Harbord whether he had any information of blood-sugar estimations in his series of cases.

Dr. Minnitt also suggested that the reason why blood-pressure findings were low after operation in the cases described by Dr. Harbord was owing to the method of anæsthesia having been a semi-closed or closed one.

Dr. Ronald Woolmer asked whether—in view of the concept of shock as acting to some extent protectively by conserving body energy, and in the light of what we knew of the beneficial effects of local cooling—the practice of applying artificial heat in shock, which was regarded as one of the cardinal principles of treatment, should be modified.

He thought that the fall in blood-pressure which occurred with high spinal analgesia was similarly protective, and his impression was that the end-results were at least as good if no attempt were made to raise the blood-pressure by the injection of vasopressor drugs. He thought there was an analogy between the application of artificial heat in cases of shock, and the artificial raising of the blood-pressure in spinal analgesia.

Dr. Barnet Solomons: In battle casualties in a jungle sector it was noted that crush and bullet injuries of the foot led to excessive shock in comparison with injuries of a greater degree in other parts of the limbs. Shock was surprisingly slight in severe injuries of the face and neck, even with much mutilation and tissue loss.

2 to 5 c.c. of pentothal in 2½% dilution was invaluable as an analgesic in anxious shocked casualties, to promote rest and quiet, and to enable a drip to be set up with ease. No further anæsthetic was administered until the general condition showed improvement

It has been stated that the "shocked" patient is very susceptible to anæsthetic drugs. The doses of these in the patients with limb or belly injuries were what would have been expected in normal patients undergoing similar operations. When the dose was deliberately reduced the depth of anæsthesia was either frankly inadequate or barely sufficient. This is contrary to what would have been expected in patients who had lost as much as 40% to 60% of their blood and had generally received insufficient transfusion. I have not witnessed operations on patients who were known to have sustained losses of more than 65% of their blood.

Of the whole series of 123 cases two belly cases died while still upon the operating table as a direct result of anæsthesia. Unfortunately I did not witness either of these cases.

The first patient had a lacerated ileum which was twenty-seven hours old. He had a general peritonitis. He became cyanosed while breathing a 4:1 nitrous oxide oxygen mixture and appeared to be deep one moment and light the next. Respirations appeared to be free but cyanosis persisted and he died in spite of intubation and artificial respiration ten minutes from the beginning of anæsthesia. Surgery had not begun. At autopsy vomit was found in the trachea and main bronchi. If this had occurred at operation it would have accounted for the cyanosis and may have contributed materially to his death.

The second patient had a large retroperitoneal hæmatoma and a bruise of the colon and he should have recovered. Anæsthesia was complicated by respiratory obstruction over a long period and the depth was not adequate. It took the surgeon seventy-two minutes to close the peritoneal cavity. The patient died about two hours from the beginning of anæsthesia. The clinical signs during most of the operation were tachycardia, hypertension, vasodilatation and sweating. The face was well coloured but was deeply cyanosed for a long time.

Disturbances of the administration of anæsthesia were frequent and were either unobserved by the anæsthetist or disregarded. Some of the 20 anæsthetists who were observed were reasonably skilful. Respiratory obstruction or hypercapnia was associated with pressor effects on the blood-pressure and vasodilatation.

Numerous examples could be quoted of cases who appeared to have some obstruction to respiration. It was especially frequent during the induction of anæsthesia and was least common with pentothal anæsthesia. In some cases it was obvious but in others insidious. The diagnosis is only certain when the respiratory movements increase at the expense of the tidal volume. Obstruction was often produced reflexly by a surgical stimulus under light anæsthesia.

Vomiting was observed during operation in 8 cases, 4 of which were limb and 4 belly cases. Pentothal anæsthesia was in progress in 6 of the cases. Vomiting was sometimes insidious, that is, it occurred without any visible expulsive effort. There were other cases which I have not included amongst the 8 who vomited at operation, e.g. 12 out of 17 pharyngeal packs used with endotracheal anæsthesia were contaminated with a fluid having the appearances of gastric secretion. Vomit sometimes produced respiratory obstruction either by setting up laryngeal spasm or by accumulating in the trachea. In one case a pulmonary abscess was aspirated about a week after operation which was related to vomiting and respiratory obstruction during anæsthesia. Other cases had pulmonary complications which appeared to be due to vomiting at operation. One case (who has not been included in the series) was witnessed who died in the induction of anæsthesia with pentothal as a direct result of vomiting and aspiration.

So frequent were these disturbances of the administration of the anæsthetic that it appeared that skill in the administration was more important than the choice of anæsthetic when comparisons were made between pentothal, ether or cyclopropane.

Section of Proctology

President—A. HEDLEY WHYTE, D.S.O., T.D., M.S., F.R.C.S.

[*November 20*, 1946]

Proctology Past and Present

PRESIDENT'S ADDRESS

By A. HEDLEY WHYTE, D.S.O., T.D., M.S., F.R.C.S.

THE dawn of the history of medicine takes us a very long way back, how far has always been in some doubt. Such authorities as Clifford Allbutt and William Osler think no further back than early Greek and Roman civilizations. The former wrote: "The medicine of Egypt and the East, extensive and intricate as it was, in so far as it is not Greek, does not contain even the rudiments of science." Sir William Osler wrote similarly: "Crude and bizarre among the primitive nations, their ideas of disease received among the Greeks and Romans a practical development worthy of these peoples. There have been systems of so-called divine healing in all the great civilizations, but for beauty of conception, and grandeur of detail in execution, all are as nothing in comparison with the cult of the son of Apollo, and of Æsculapius, the god of healing."

"Scientific medicine, the product of a union of religion with philosophy, had its origin in a remarkable conjunction of gifts and conditions among the Greeks in the sixth century."

"Facts regarding the ancient history of medicine have been sought for only in the classical authors of Greece and Rome, and have been arranged to suit a traditional theory which repudiated all systems which did not proceed from a Grecian source. We are familiar, from our youth, with classical history, and we love to recall events illustrated by the torch of Genius, and depicted in our memories."

But still candour and truth require us to examine new facts in history as they are discovered, and we must try and arrive at just conclusions.

In what has modestly been termed a monograph, published in Calcutta in 1913 [1], there is a wonderful description of old Hindu surgical instruments, with a comparative study of the Greek, Roman and Arab surgeons with the surgeons in modern times. There is little doubt that Indian medicine was advancing from consisting merely of spells and incantations against the demons of disease.

In 226 B.C. King Asoka [2] records the erection of hospitals by him, and Cingalese records indicate the existence of hospitals in Ceylon as early as 437 B.C.

One of the great Brahminical works is the Susruta (fifth century A.D.), a great storehouse of Aryan knowledge. Susruta recommends lotus leaves and plantain leaves as coverings to bleeding piles, and also the application of caustics to them. If these measures were not efficacious then he applied horse-hair ligatures round the piles. There are reasons for thinking that, contrary to the oft-expressed opinions of our betters, Greek medicine and thought may really have been founded on the more ancient Hindu medical doctrines. We know Alexander was not satisfied with his own Army surgeons, and had to take several Indian ones on to his Staff. These later he took back to Greece with him, and, in this way, there is every possibility that their knowledge and practice might have germinated in their new country of adoption.

So much for the ancient period which ends with Galen (131-202) who explained all in the light of pure theory, and such was the effect of his dogmatism and infallibility, that European medicine remained at a dead level for nearly fourteen centuries.

Dr. H. W. Loftus Dale said he would be interested to hear what observations the openers had to make concerning two techniques which had not been mentioned, refrigeration anæsthesia and curare.

He had, himself, used the former on five occasions for amputations of the lower limb in very poor risk cases, and had been impressed by the fact that there had been little or no alteration in pulse or blood-pressure, and no further deterioration in the patient's general condition, trauma to the great sciatic nerve had produced no noticeable effect.

Concerning curare, he would be interested to learn if there was any explanation for the fact that severe operations such as abdomino-perineal excision of the rectum and partial gastrectomy could be performed in light planes of general anæsthesia with the help of curare—which produced no sensory loss—without the production of shock.

Dr. Stanley Rowbotham (President) thanked Professor Green and Dr. Harbord for their valuable papers; shock was a condition which the anæsthetist encountered only too often, and about which he could never learn too much. To-day they had gained a great deal of very valuable knowledge.

He agreed with Professor Mackintosh that " In shock a little anæsthetic goes a long way". He well remembered the case of a wounded German soldier with advanced peritonitis who died after receiving only 1 c.c. of 5% pentothal.

He had been greatly impressed by intravenous procaine in cases of severe burns, which he had seen used by the Canadian Medical Corps during the war. He had himself given it to two cases; both were rendered free of pain within about five minutes and the pulse straightway improved.

Dr. R. P. Harbord, in reply to Dr. Minnitt, said that the blood sugar had not been estimated in the cases under review. To Dr. Loftus Dale he said that he had no practical experience of refrigeration anæsthesia but that he could produce evidence of deterioration at operation when curare was used. To those who felt that "in shock a little anæsthetic goes a long way" he said that it all depended on what was meant by the word "shock". If a patient was on the brink of death it might be that the slightest push would send him over but it should be rare to have to anæsthetize such a patient.

Professor H. N. Green, in reply to Dr. Woolmer, said it was becoming more widely recognized that artificial heat, as a general rule, was not desirable in the treatment of shock. A physiological concept of shock would suggest that the body temperature should be allowed to reach its own level without artificial aid in either direction. From this point of view general cooling might be just as harmful.

To Dr. Loftus Dale he said, that from the experimental standpoint, refrigeration anæsthesia for amputation of the lower limb should be ideal. If shock in such cases were in a broad sense metabolic in origin local cooling would have a pronounced retarding effect on such changes, and also prevent the release into the general circulation of any metabolic factors formed.

If, in fact, shock did not occur with curare and light general anæsthesia it would be in line with the experimental evidence showing that, with an intact spinal cord, uncomplicated sensory nerve stimulation did not produce shock. Evidence was accumulating that stimulation of motor nerves might induce the metabolic changes associated with shock and I am now investigating whether curare has any prophylactic effect in experimental shock.

were being founded everywhere. Major surgical operations were being attempted, and to mention two examples, in 1808, an inter-scapulo-thoracic amputation was performed, and the first ovariotomy in 1809.

Fortunate in the time of his birth, was one Frederick Salmon, destined to be the father of proctology, and the founder of such a unique and famous hospital. Salmon was born in Bath in 1796. He received his medical education in St. Bartholomew's Hospital, and in 1827 he was elected surgeon to the General Dispensary in Aldersgate Street. He early interested himself in rectal diseases, and in 1835, in spite of a good deal of professional opposition, he acquired premises at 11, Aldersgate Street. This was "The Infirmary for the Relief of the Poor Afflicted with Fistula and Other Diseases of the Rectum".

Salmon was a great man who did great work. For twenty-two years he did the surgery of the hospital single-handed. Nine years after the hospital opened, he acquired a medical colleague, one John James Furnivall.

In 1838, a move was made to Charterhouse Square, and this meant the number of beds was doubled. In 1854, on St. Mark's Day, April 25, the hospital on the present site in City Road was opened with at first 25, and five years later, 30 beds. In 1927, the hospital was still further extended.

Three years after the move to City Road, Salmon was assisted by James Robert Lane and Peter Yeames Gowlland, and, in 1859, Salmon retired full of honour, and well beloved by all. He left for proctology, a great name, a great hospital, a book, his "Practical Treatise on Stricture of the Rectum", and his ligature operation, so well described by William Allingham in his textbook "Diseases of the Rectum" (1888).

Lane and Gowlland followed Salmon—Lane only stayed at St. Mark's 11 years. Meantime he had been appointed one of the original members of St. Mary's Hospital, and been unfortunate enough to develop locomotor ataxia. We read that in the prime of his life, and when a career of prosperity appeared to be within his grasp, he was stricken with this painful malady. In spite of being attended by agonies, which at times rendered his condition almost unendurable, he worked at St. Mary's until 1881.

This mid-Victorian era was a golden one for surgery, and I trust, surgeons too. We must always orientate our thinking in this period of surgical history around 1867, when Lister [9] published his article in the *British Medical Journal*, "On the Antiseptic Principle in the Practice of Surgery", remembering also the discovery of general anæsthesia some twenty years earlier.

It was an era with great surgical masters, and as early as 1844 Lee and Hay had successfully resected a part of the sigmoid colon for cancer. There were no further successes until the 1870s, when German surgeons adopted Lister's antiseptic technique, and began to attempt all sorts of formidable operations within the abdomen. Several of them shortly attempted to resect cancers of the colon, but probably the first to succeed was Vincent Czerny, Professor of Surgery at Heidelberg [10].. After several failures, he brought a patient through the procedure alive in 1879. By 1884 a total of 18 such operations had been done with 8 fatalities. The next generation saw great improvements in the technique of bowel resection. The really important advance came, however, with experimental studies carried out on dogs by William S. Halsted at Johns Hopkins Hospital. In 1887, in a series of careful experiments, he proved that the essential point in suturing the bowel is to include the submucous layer of the intestinal wall in the suture.

The surgical problem of cancer of the rectum is a more difficult one. Jacques Lisfranc, a brilliant Parisian surgeon of the Napoleonic period was the first in 1826 to excise the rectum for cancer. His resection, however, was of very limited extent, Oribasius [3] was another writer with an enormous amount of literature associated with his name. He was friend and physician-in-ordinary to Julian the Apostate in Constantinople, and was chiefly responsible for establishing Galen in his central position of authority during the Dark Ages.

Oribasius was a great compiler, and he twice mentions piles, suggesting that when treating them, one pile should always be left, otherwise the consequences might be dangerous. It is interesting to think how to this day a sort of feeling of security may be had by a patient with a bleeding pile. One often hears expressed the remark that it may be a safety valve against apoplexy, or, better have bleeding there than in the brain. Also too, there may be a lurking suspicion of dignity and aldermanic pomp associated with piles, and certainly often they enforce a steady, measured gait. With one or two exceptions, the medical world seems to have gone to sleep for centuries after Galen, and Osler has said: "From Hippocrates to Hunter, the treatment of disease was one long traffic in Hypotheses."

I would say it is a long stride from ancient Greece to a "small room in Aldersgate Street." [4]

In our jet-propelled flight through darkness, we notice *en passant*, only an odd proctological happening, a flash in the pan, as it were.

The greatest of the Moslem physicians of the Western Caliphate was the Cordovan Avenzoar [5], who died at Seville in 1162. He discovered the *Acarus scabiei*, was a great physician, and a great man. He cared nought for Galen, and it is interesting to know that he gave nutrient enemata to his patients with carcinoma of the stomach, and for those with carcinoma of the œsophagus, he passed a hollow metal tube through the growth, and through the tube he fed his patients on milk, eggs and gruel. When giving rectal feeds, he first washed out the lower bowel, and then he filled a goat's bladder, fastened a tube to it, and having inserted the tube into the rectum, the goat's bladder was emptied by compression.

The story of John Aderne of Newark is well known, thanks to the researches of D'Arcy Power and the Wellcome Research Institution. You have all seen the pictures of the fistula being split up. That was in 1376, and you have all read Gordon-Watson's delightful address, which he gave at St. Bartholomew's in 1934. If perchance there is anyone in this audience who has not read Sir Charles' "Progress in Rectal Surgery" [6], then he has a treat in store. Aderne's "Principles and Practice" must have soon been forgotten, for our Henry V died of fistula only forty-six years after Aderne's classic operation, because, we are told, "the surgeons had not the skill to cure." Rectal surgery, indeed all surgery, continued to occupy a very lowly position until the early part of the last century. Except for the famous operation by Félix on Louis in 1686 [7], and Percival Pott's treatise on fistula in 1765, there is little to make us pause. We want to get on and hear about St. Mark's, but I must first tell you the story about Félix and Louis XIV. At that time, French surgeons were little thought of by their more superior medical brethren, and all were more or less looked on as social inferiors.

Molière's comedies abounded in pungent raillery and light-barbed sarcasm directed with unerring skill against the tribe of doctors. In 1657, as luck would have it, when doctors were so little thought of, Louis had an attack of typhoid. He was treated with antimony and he recovered. This recovery raised the status of the profession in France, and also caused an immense vogue for the use of antimony. Six years later, his mistress was attended by the Royal accoucheur, a man, and this event did much to further the cause of male midwifery.

Louis' recovery from his attack of typhoid, and the successful delivery six years later by an obstetrician, much as these events tended to increase the standing of the profession, within the profession, the relative standing of the surgeons tended to be lowered by comparison, but in course of time they had their opportunity. In 1686, Félix opened up the King's fistula. The King was cured, and surgical times changed. Félix received six thousand pounds as a fee, and, what some of us might now think a very suitable refresher, he was also given a present of a farm. Félix was ennobled, becoming Seigneur de Stains. All his helpers received financial recognition in proportion. Félix was followed by Mareschal. Fistula became fashionable, and this, together with the exertions of Mareschal, put French surgery into the foreground.

Littré in 1710 first proposed colostomy for the relief of imperforate anus, but it is doubtful whether he ever performed the operation.

In 1776, Pillore of Rouen performed cæcostomy in the right iliac region for the relief of obstruction in an adult case, and four more cases were recorded before the end of the century, three for imperforate anus, and one of transverse colostomy. The transverse colostomy was inadvertently performed when a laparotomy was being done, with the intention of opening the small bowel.

In 1797, one Pierre Fine [8] (1760-1814) performed colostomy for intestinal obstruction in an adult, and we read that the patient survived for three and a half months.

The surgical dawn seemed to be breaking, and it is interesting to recollect that our College obtained its Royal Charter in 1800. Truly the early years of the last century saw great surgical and academic advances. Universities and hospitals

Goodsall certainly left his mark on Surgery, and his co-author, of course, has already done so. We know so much about Ernest Miles, but some of us perhaps do not know enough about Goodsall. His early life was hard. His father had died of a post-mortem wound infection when he was a student at St. Bartholomew's. and Widow Goodsall was left with four sons unprovided for. From the age of 14, D. H. kept himself and was apprenticed to a chemist at Aldgate. In view of his father's misfortune, St. Bartholomew's took him in, and he was allowed to pursue his medical studies, without having to pay any fees. He became in time a house surgeon at St. Mark's, and later surgeon there and at the Metropolitan Hospital. He recognized post-anal dermoids [13], and knew how to treat them by completely laying all the tracks open, whereas previously it had always been supposed they were a bone infection. It was John Bland-Sutton, of course, who told of their true nature, and Percy Lockhart-Mummery [13] who taught us to excise them completely. Mention of Miles naturally necessitates mention of Lockhart-Mummery. Since the turn of the century, what controversy raged about the adequate treatment of rectal carcinoma. Hartmann in Paris we associate with abdominal excision.

Many surgeons, the masters at St. Mark's and all over the world, were doing more and more and larger excisions. In Newcastle, Rutherford Morison, and later George Grey Turner, and in Rochester, the Mayos. The list is wellnigh inexhaustible. Great progress was made, but in January 1907 [14], Ernest Miles did his first abdomino-perineal excision, one of the most formidable operations in surgery. Miles described the operation, and explained what we now take so much for granted, the three zones of spread.

Miles ascribed an abdomino-perineal excision to Czerny in 1884, and after that to many others—Maunsell, Gaudier, Gant, Tuttle, Reverdin, Sir Charles Ball, Wallace and Aldrich-Blake—but it was not until he had thoroughly worked out the methods of spread that Miles was able properly to plan his operation similar in conception to Halsted's radical excision of the breast, and Wertheim's excision for uterine cancer. As Miles says with just pride in his "Rectal Surgery" in 1944: "The operation reduced the recurrence rate from 90% to 20%." It must surely be more than coincidence that the article directly in front of Ernest Miles' is by one Lionel Norbury. He was then a Registrar at St. Thomas's Hospital, and the article was on "A case of ruptured small intestine". The abdomino-perineal excision done by others than Miles had a very high mortality, and abdominal resections were favoured by Harrison Cripps (1907) and William Mayo (1912), and again by Hartmann in 1923. Lockhart-Mummery, except for high growths, always favoured an extended operation through the perineum.

George Grey Turner [15] in 1920 described a two-stage perineo-abdominal excision, and, in 1931, his classic Murphy oration on conservative sacral excision revived interest in less extensive operations than that of Miles'. Miles, however, won the day. As our mortality rates decrease as the result of experience, better technical understanding, better anæsthesia and modern resuscitation, more and more extensive excisions are performed. Well I remember the times when I used to assist my colleague and assistant chief, the late much-lamented Hamilton Drummond, and how gratified we were when the patient survived. Now, of course, a fatality is cause for comment, and perhaps recrimination. Gabriel's reverse method [16], and the synchronous combined operation described by O. V. Lloyd-Davies in 1939 [17] have largely taken the place previously occupied by Miles' operation. The advantages of the synchronous procedure so well detailed by Norbury in his Hunterian Lecture in 1941 are: (1) No necessity for moving the patient after he is once fixed in the required position. (2) The time taken over the operation is considerably diminished. (3) Growths adherent and which by other means would be considered inoperable may be successfully removed. (4) In selected cases a conservative recarried out through the perineum. The scope of this perineal resection was gradually extended after antiseptic surgery made extensive operations safer. In 1885, Paul Kraske, Professor of Surgery at Freiburg, introduced a method in which a portion of the sacrum was removed to give better access. The operation was widely used for more than a generation. Unfortunately, it had the same defect as other exterior or perineal operations for rectal cancer. The recurrence rate approximated 90%.

During this great time going forward with the great surge, we can imagine William Allingham, Alfred Cooper, David Henry Goodsall, F. Swinford Edwards, Herbert William Allingham, Frederick Charles Wallis and Percy Furnivall working away at St. Mark's. They all made their marks, some deeper than others, and all left "Marks" better for their passing that way.

Piles, fistulæ, fissures, prolapse, stricture and carcinoma. What discussions there were. We have the classical papers of William Allingham on the treatment of fistulous sinuses by the elastic ligature, on inguinal colostomy and piles.

Sir Alfred Cooper's classic on inflammation of the rectum, D. H. Goodsall's papers on foreign bodies in the rectum, six cases of sinuses over the sacrum and coccyx and on fissure all these, and many more equally interesting and instructive, are preserved and beautifully presented for us in the St. Mark's Centenary Volume.

Take the subject of colostomy alone—colostomy or colotomy—the varieties thereof, and the technicalities of the operation.

As mentioned before, Pierre Fine had performed colotomy in 1797. Three more were done in 1814, 1817 and 1820.

Between 1839 and 1841, Amussat [11] wrote and popularized lumbar colostomy. His first cases were on the right side, and the opening made into the ascending colon. As time went on, many cases were reported, many more in this country than in the United States of America, where there was considerable opposition to the operation. Gross in his "System of Surgery" apologizes for even mentioning the operation.

During this time Paul was practising in Liverpool and perfecting his classical exteriorization and Mikulicz was trying to extend its usefulness in Vienna.

The injection treatment of piles [12], which had so long been frowned upon by the orthodox, was being tried out more and more. In the United States of America in 1836, Long injected sulphate of iron into a nævus. In 1869 Morgan in Dublin tried the same treatment with hæmorrhoids, and in 1874 Colles used perchloride of iron. In 1871 Mitchell of Colindale in Illinois had first used carbolic acid in two parts of olive oil. As the result of his method becoming known, he apparently became so busy that he could not attend to all his patients, and, it must be noted with regret, he sold his secret prescription. As our present Minister of Health might say, there was a "rash" of pile injectors all over the country. With the orthodox, the method, therefore, fell into disrepute, but later was revised by Andrews of Chicago and others. The strong solutions gave way to weaker ones with more satisfactory results.

After the early 1800s had seen such great surgical progress, so were the last years of the century to witness equally epoch-making advances. Towards the end of the century, Goodsall, whose name to this day is associated with his line and his stitch, was writing his book. He was assisted in his literary endeavour by a young surgeon who had been a house surgeon at St. Mark's, and who was then assistant surgeon at the Cancer Hospital, and surgeon to outpatients at the Gordon Hospital. What a wonderful combination, David Goodsall and Ernest Miles. Their book was published in 1900, with a second edition published in 1905, which contained a classical article on colostomy. They also well described the operations for rectal cancer being done at that time.

Section of Comparative Medicine

President—G. R. Cameron, F.R.C.P., F.R.S.

[*December 4, 1945*]

Studies on the Hæmatology of the Horse, Ox and Sheep

By H. H. Holman, D.Sc., Ph.D., M.R.C.V.S.

Early workers in veterinary hæmatology all appear to have concentrated on determining the correct average for the different constituents of blood, and even as late as 1935 one writer, in a review article, used the results obtained by several investigators in an attempt to standardize averages for such estimates as the erythrocyte counts for farm animals. This worker considered that 6·6 million erythrocytes per c.mm. could be accepted as the true average for the ox but, unfortunately, this knowledge is of little value to the clinician or the experimental pathologist in deciding whether a cow with a count of only 5 million should be accepted as normal or should be considered as suffering from some degree of anæmia. Therefore in clinical work and experimental work, what is important is not the average but the normal range for the healthy animal; and that is where veterinary literature gives one so little help.

Early investigators usually employed small groups of animals all in the same flock or herd and restricted their results to the average, or the average together with the maximum and minimum—that standard that Yule has called "The worst of all possible measures for any serious purpose"—and to explain their results it is to be feared that in some cases figures that seemed to fall at too great a distance from the mean were omitted as due to "experimental error".

The result of such omissions is reflected in those textbooks and articles that publish the averages for the various counts as the normal for various animals but stipulate that figures within 10% on either side may be accepted as samples from healthy animals. The work of Berkson, Magath and Hurn (1940) and of Berg (1945), has confirmed that even in the red count, where the error is less than in either the absolute or relative leucocyte count, the distribution error alone can easily account for ± 10%. Thus, admitting only counts within 10% of the means as normal, it should be quite possible to show some animals to be suffering from anæmia one day and anhydræmia the next or to show that most healthy animals varied from leucopenia to leucocytosis several times a week.

In this country the first real attempt to establish the normal range for the sheep and the ox by using the standard deviation was made by Fraser (1930), but unfortunately his efforts were restricted in numbers and with regard to season and environment. Nevertheless he showed that variation between healthy animals was extensive and established a paradox by showing that improved mathematical interpretation widened, rather than narrowed, the normal range.

Histograms for sheep sampled between June and December show the wide distribution; the red count varies from a class with a centre point of 6·5 to one with a centre point 15·5 million per c.mm. The distribution of the white count is remarkably irregular, varying from the 2,000 class to the 14,000 class with one animal isolated at 18,000 per c.mm. Eosinophils and basophils are both skewed to the right, in fact basophils show the mode at zero.

We know that with worm infestation there is a neutrophilia, an eosinophilia in benign cases and a tendency to anæmia, so that when we see that the distribution for both neutrophils and eosinophils is skewed to the right and that for hæmoglobin is skewed to the left, it does suggest that although we begin by choosing apparently healthy animals to record their blood picture, we can end by using the blood picture to suggest that many of these animals were not healthy. In spite of this there appears to be no remedy, for it is the animal free from worm infestation section of the recto-sigmoid is rendered easier. These advantages make this method the one of choice with most modern surgeons.

Personally I have a sneaking affection for what I call my extended Hartmann which is an abdomino-perineal, which stops short, as it were, and preserves the perineum. I don't believe in the downward spread, but that can wait for another time.

Modern resuscitation methods have been mentioned. You all know Officers apparatus. "An important and erudite contribution on the physiology of water balance and the problems associated with the administration of fluids" is how Gabriel rightly describes Avery Jones and Naunton Morgan's article in St. Bart's Hospital Reports in 1938 [18]. With our facilities, all we want is our patients earlier. The outlook in rectal carcinoma becomes better each year, and who knows what advances lie ahead. We remember Gordon-Watson's enthusiasm in the late twenties with radium, and how we followed him, and like him, were disappointed; but perhaps the physicists may have something to give us soon.

Mention must be made of Milligan's pile operation [19], correct anatomically, and a great advance on Salmon, Smith and Whitehead. Also we are indebted to Milligan and Morgan for their anatomical work [20] and their classification of fistula.

Purposely I have kept till the last my tribute to Cuthbert Dukes. His work since 1922 at St. Mark's on all problems connected with the pathology and biochemistry of rectal disease is known the world over. His apparatus for the post-operative collection of urine is universally used. He has elucidated the relationship of simple tumours to intestinal cancer. His work on rectal stricture rivals Bensuade's in importance, and, with Broder's classification of malignant tumours based on the principle of cell differentiation, his method of classification by extent of spread has enabled us scientifically to grade and classify our cases.

REFERENCES

1 Mukhopadhyaya (1913) The Surgical Instruments of the Hindus. Calcutta.
2 Garrison, F. H. (1913) History of Medicine, p. 70. Philadelphia.
3 Daremberg (1862) Œuvres d'Oribasius, 4, 1862, Paris.
——, (1873) Œuvres d'Oribasius, 5, Paris.
4 Collected Papers of St. Mark's Hospital 1835 to 1935 (1935) London.
5 Robinson, V. (1931) Story of Medicine. New York.
6 Collected Papers of St. Mark's Hospital (1935) London, p. 394; and *St. Bart's Hosp. J.*, 1934, 41, 104.
7 Garrison, F. H. (1913) History of Medicine, p. 295. Philadelphia.
8 Fine, P. (1805) *Ann. Soc. Méd. Montpellier*, 4, 34 to 54.
9 Lister (Lord) (1867) *Brit. med J.* (ii), 246.
10 Haagenson, C. D., and Lloyd, W. E. B. (1943) One Hundred Years of Medicine. New York.
11 Amussat, J. Z. (1839-43) Trois Mémoires sur la possibilité d'établir un anus artificiel dans le région lombaire sans pénétrer dans le péritoine. Paris.
12 Anderson, H. G. (1924) *Practitioner*, **113**, 6.
13 Lockhart-Mummery, J. P. (1921) *Brit. med. J.* (i), 807.
14 Miles, E. (1908) *Lancet* (ii), 1812.
15 Turner, G. Grey (1920) *Brit. med. J.* (ii), 734.
16 Gabriel, W. B. (1932) Rectal Surgery. London.
17 Lloyd-Davies, O. V. (1939) *Lancet* (ii), 74.
18 Jones, F. A., and Morgan, C. N. (1938) *St. Bart's Hosp. Rep.*, **71**, 83.
19 Milligan, E. T. C., *et al.* (1939) *Brit. med. J.* (ii), 412.
20 ——, and Morgan, C. N. (1934) *Lancet* (ii), 1150 and 1213.

Section of Comparative Medicine

President—G. R. Cameron, F.R.C.P., F.R.S.

[December 4, 1946]

Studies on the Hæmatology of the Horse, Ox and Sheep

By H. H. Holman, D.Sc., Ph.D., M.R.C.V.S.

Early workers in veterinary hæmatology all appear to have concentrated on determining the correct average for the different constituents of blood, and even as late as 1935 one writer, in a review article, used the results obtained by several investigators in an attempt to standardize averages for such estimates as the erythrocyte counts for farm animals. This worker considered that 6·6 million erythrocytes per c.mm. could be accepted as the true average for the ox but, unfortunately, this knowledge is of little value to the clinician or the experimental pathologist in deciding whether a cow with a count of only 5 million should be accepted as normal or should be considered as suffering from some degree of anæmia. Therefore in clinical work and experimental work, what is important is not the average but the normal range for the healthy animal; and that is where veterinary literature gives one so little help.

Early investigators usually employed small groups of animals all in the same flock or herd and restricted their results to the average, or the average together with the maximum and minimum—that standard that Yule has called "The worst of all possible measures for any serious purpose"—and to explain their results it is to be feared that in some cases figures that seemed to fall at too great a distance from the mean were omitted as due to "experimental error".

The result of such omissions is reflected in those textbooks and articles that publish the averages for the various counts as the normal for various animals but stipulate that figures within 10% on either side may be accepted as samples from healthy animals. The work of Berkson, Magath and Hurn (1940) and of Berg (1945), has confirmed that even in the red count, where the error is less than in either the absolute or relative leucocyte count, the distribution error alone can easily account for ± 10%. Thus, admitting only counts within 10% of the means as normal, it should be quite possible to show some animals to be suffering from anæmia one day and anhydræmia the next or to show that most healthy animals varied from leucopenia to leucocytosis several times a week.

In this country the first real attempt to establish the normal range for the sheep and the ox by using the standard deviation was made by Fraser (1930), but unfortunately his efforts were restricted in numbers and with regard to season and environment. Nevertheless he showed that variation between healthy animals was extensive and established a paradox by showing that improved mathematical interpretation widened, rather than narrowed, the normal range.

Histograms for sheep sampled between June and December show the wide distribution; the red count varies from a class with a centre point of 6·5 to one with a centre point 15·5 million per c.mm. The distribution of the white count is remarkably irregular, varying from the 2,000 class to the 14,000 class with one animal isolated at 18,000 per c.mm. Eosinophils and basophils are both skewed to the right, in fact basophils show the mode at zero.

We know that with worm infestation there is a neutrophilia, an eosinophilia in benign cases and a tendency to anæmia, so that when we see that the distribution for both neutrophils and eosinophils is skewed to the right and that for hæmoglobin is skewed to the left, it does suggest that although we begin by choosing apparently healthy animals to record their blood picture, we can end by using the blood picture to suggest that many of these animals were not healthy. In spite of this there appears to be no remedy, for it is the animal free from worm infestation that is an abnormal farm animal, and if one is to restrict sampling to such abnormal animals, the clinical value of the result is negligible.

The wide range for most constituents in farm animals, although it permits one to judge a flock or herd of animals, is useless in judging small changes in the individual animal. If, therefore, we are interested in experimental pathology, we must try to devise some criterion for limiting the normal range as regards an individual; this I have attempted to do by introducing what Dr. Kermack of Edinburgh—who was kind enough to help me—termed the Maximum Admissible Difference.

This parameter is obtained by bleeding animals at the same time on two consecutive days and finding the difference for each constituent. These differences are used to calculate the standard deviation and the table of "t" is then used to find the area covering 95% of the possibility. Thus the M.A.D. for the daily variation in the red count is rather less than ± 3 million, so that if we bleed a sheep with a count of 15 million and the next day the count has fallen to 10 million, then although the new figure is well within the normal range, it is outside the M.A.D. for daily variation, and it is reasonable to assume that the fall is unlikely to be due only to experimental error and daily variation. This may appear to some people to be an abuse of mathematics but—bearing in mind that no biological test is 100% perfect —I have found it a useful and reasonably reliable standard.

The figures for the herbivorous farm animals are shown in the table with the figures for each constituent given as the mean and the standard deviation.

AVERAGES AND STANDARD DEVIATIONS

Leucocytes

Species	Total 10^3 p.c.mm	Differential count			
		Neutros.	Lymphos.	Monos.	Eosinos.
Horse	9·0 ± 1·6	58 ± 12	29 ± 11	5 ± 2·5	7 ± 3·5
Ox	8·0 ± 2·0	30 ± 10	52 ± 15	7 ± 4·0	10 ± 7·0
Sheep	9·2 ± 3·1	24 ± 9	68 ± 10	3 ± 2·7	4 ± 4·5

Erythrocytes

Species	Count 10^6 p.c.mm.	Hb. g./100 ml.	Corp. Vol. %	M.C.V. c. micra	M.C.H.C. %
Horse	7·0 ± 0·7	10·0 ± 1·5	28 ± 3·5	40 ± 4	35·5 ± 3·0
Ox	6·0 ± 1·3	11·8 ± 1·3	28 ± 3·5	49 ± 6	33·1 ± 3·5
Sheep	11·5 ± 1·8	12·4 ± 1·4	29 ± 4·0	27 ± 4	41·1 ± 4·0

In the table the sheep has an average of 11·5 million per c.mm. erythrocytes, roughly twice the human figure. The corpuscular volume is only 29%, giving us a total cell size of 27μ^3, about one-third the size of the human corpuscle. Although the other herbivorous animals have somewhat lower red counts, the corpuscular volume and the hæmoglobin concentration is about the same for all three.

In addition to the points shown by the table, there are other interesting differences. For example, the sedimentation rate in the horse is much faster, with a fall of about 4 cm. in fifteen minutes, than in ruminants where the fall may be almost unobservable even after twenty-four hours. This quick sedimentation in the horse is combined with a tendency for the corpuscles to form rouleaux and if a direct method of hæmoglobin estimation is employed, such as the Dare method, the formation of rouleaux may produce a field of scattered red specks. Hæmoglobin is also difficult to estimate by the ordinary Sahli method for at the dilution given by this method, the horse's hæmatin is too blue a brown to match the human standard. Cow's blood is also difficult to estimate by a direct method using a human standard, for it is too yellow. This yellow tinge may be due to the yellow colour of the plasma which cannot be estimated by standards employed for the human icteric index.

Besides the differences in erythrocyte size and numbers, there is a difference between the animals in erythrocyte regeneration. Wirth (1938) investigated this by bleeding animals until the red count was reduced to half and then examining the blood for regenerative changes. He found no reticulocytes in the horse and other regenerative changes were scarce. On the other hand, in the sheep reticulocytes were numerous with large numbers of polychromatic cells and many cells showing punctate basophilia. Thus both these herbivorous animals form a contrast to the dog and cat, where Jolly's bodies and nucleated red cells are the predominant change.

Neser (1923) has shown that the horse has another characteristic, for if it is excited the red count may show an increase of 1 or 2 million within a few seconds, and this suggests an easy way of rectifying a slight oligocythæmia.

The average leucocyte counts for herbivorous animals are all about 8,000 per c.mm. in contrast to other domestic animals, particularly the cat with an average of over twice this number. Figures for neutrophil percentage show that the horse is similar to man, having roughly double the number of neutrophil cells to lymphocytes, while in the ruminants this ratio is often reversed.

Cell types are similar to those in man. In carrying out differential counts the difficulty with ruminants lies in distinguishing between monocytes and large lymphocytes, in contrast to the horse where the difficulty during a neutrophilic reaction is to distinguish between monocytes and metamyelocytes. The most striking blood cell among all the domesticated animals is undoubtedly the eosinophil of the horse. If this cell is stained by Leishman, instead of seeing chunks of material stained eosin red, one sees a cell containing large orange globules giving it a most spectacular appearance. No one has attempted to explain the difference between this cell and the more common type of eosinophil but anyone attempting to work on a histochemical analysis of eosinophils would do well to include that of the horse.

Finally, there is one important difference between human blood and the blood of domestic animals, of great clinical importance. Hæmatology textbooks appear to avoid a direct statement on the matter, but in man there does not seem to be any line of demarcation between band forms and what can be called under the Cooke and Ponder count, a "Poly. I". In several of the domestic animals, "Poly. I's", resembling Schilling's "degenerative band forms" or Osgood and Ashworth's (1937) cells 78 and 79, are common and variable, on one day representing the majority of neutrophil cells and on another a small minority. If one includes these cells as band forms when carrying out a Schilling Index or some similar index, all sensitivity is lost, therefore in farm animals it is very necessary to ensure that one restricts the band forms to very definite metamyelocytes with a simple bandlike nucleus.

REFERENCES

Berg, W. N. (1945) Blood Cell Counts, *Amer. Rev. Tuberc.*, **52**, 179.
Berkson, J., Magath, T. B., and Hurn, Margaret (1940) *Amer. J. Physiol.*, **128**, 309.
Fraser, A. C. (1930) *First Rep. Inst. Anim. Path. Univ. Camb.*, p. 114.
Neser, C. P. (1923) *Ninth and Tenth Rep. vet. res. S. Afr.*, p. 479.
Osgood, E. E. and Ashworth, Clarice M. (1937) Atlas of Hæmatology, San Francisco.
Wirth, D. (1938) Rep. 13th int. Vet. Congr. 1, 273.

The Serum Proteins of the Domestic Animals

By John B. Brooksby, M.R.C.V.S.

My own experimental work on the normal serum proteins of the domestic animals is limited to studies on the ox and pig, and to complete the picture I have to rely on observations taken from the literature. I should, however, like to draw attention to several factors which obscure the comparative aspects of this subject.

The first of these is that the greater part of the data available in the literature is the by-product of other research. Observations have frequently been limited to those essential for the particular work in hand, and have not been extended to yield complete information on the normal. The second factor which complicates the comparative study is a technical one. With the development of protein chemistry new methods of characterization of the serum proteins have been discovered. The multiplicity of "salting-out" methods, and the variations resulting from what may seem minor changes in technique, have been considered in many of the earlier papers, notably in the review by Howe (1925). It appears likely that the existence of several different estimates for the protein fractions in any particular species is, in part, due to technical points such as those raised in the papers referred to. This situation does not render easier the comparison of species with species.

Just as in salt-fractionation, small differences in technique make for wide discrepancies in the results obtained by the methods of electrophoresis and ultracentrifugation. In electrophoresis, the pH, the buffer used, and the ionic strength of the medium greatly influence the apparent constitution of the serum. In ultracentrifugation, the dilution of serum used is an important factor and specification of the conditions of experiment is therefore essential to the presentation of results.

No comparison is yet available for salt and electrophoretic analyses made side by side on the same series of animal sera. Such comparisons do exist for human sera, and it is interesting that the proportion of protein assigned to albumin is generally higher for the salting-out method than for the electrophoretic. Figures for the relationship are given by Taylor and Keys (1943) for eight normal sera. The mean percentage of albumin in these sera was 71·4 by the salt method, while electrophoretic analysis gave a value of 65·9. The discrepancy appears to be even greater for pathological sera. Until similar figures are available for the sera of the domestic animals, we can compare only the normals established by different workers using the different methods.

The third factor which makes data for comparison difficult to obtain from the literature is that, in comparing the results of different authors, we are particularly at the mercy of variations in the animals studied, in respect of breed, age, sex, condition and so forth. Little is known of the effects of these factors in the sera under consideration, except in the outstanding case of the deficiency of the sera of the young ruminants in the orthodox globulin fractions. Less striking differences in the animals studied may add to the confusion between authors.

The values so far reported for bovine serum albumin expressed as a percentage of the total serum protein illustrate well the variations from author to author. They are 48% (Howe), 44% (Hartley), 47% (French), 54% (Brooksby), and 55% (Hewitt). These values were obtained by the "salting-out" method, using ammonium sulphate, sodium sulphate, or sodium sulphite. The value given by Svensson (1946) based on the electrophoretic analysis of ten sera is 41%.

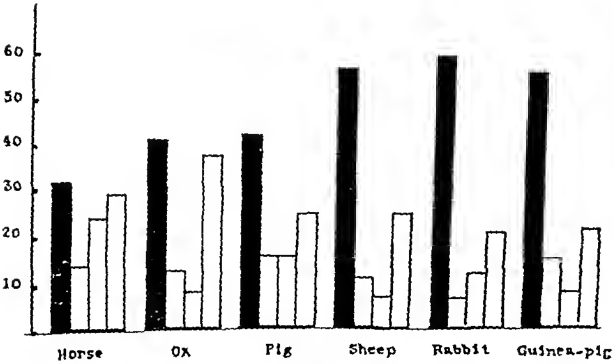


FIG. 1.—Percentage of total serum protein in electrophoretic fractions (for details see text).

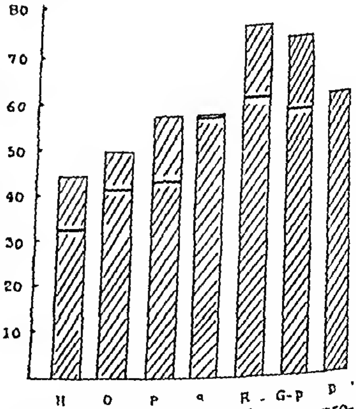


FIG. 2.—Percentage of total serum protein accounted for by albumin in various species. ("Salting-out" data.)

As the only data collected by one worker on the sera of several domesticated animals are those of Svensson referred to above, the above diagram (fig. 1), which I have prepared from the results given in the monograph, probably represents the best information on the differences which exist between the species concerned.

For each species, the first (shaded) column represents the albumin, and the others respectively the α β and γ globulins, each as a percentage of total serum protein. Comment on the wide differences between species does not seem necessary.

I have been unable to find a similar research by one observer on the "salting-out" of the fractions from the sera of different species. This seems an unfortunate gap in our knowledge, for, as is plain from the list of values for bovine serum albumin shown earlier, the observations of different workers on the same species may vary by as much as the species do among themselves. The next diagram (fig. 2), therefore, is a composite one, which I have prepared from the results of all the "salting-out" experiments on the sera of the species concerned, which I have encountered in the literature. The columns represent the percentage of the total serum protein accounted for by albumin in the sera of, respectively, horse, ox, pig, sheep, rabbit, guinea-pig, and dog. The line drawn across each of the first six columns shows the percentage of albumin estimated by the electrophoretic method, and this figure is taken from Svensson's results. The general trend of the "salting-out" results is thus the same as the electrophoretic, the greatest discrepancy is in the ovine serum, where, instead of the value by electrophoresis being 5 to 10% lower than the "salting-out" value, the two correspond closely. Otherwise, the results suggest that the relationship demonstrated for human serum also holds for animal sera.

I have not included the salt-fractionation of the globulins in this table, as even greater variations occur from author to author. My own estimate of the euglobulin for the cattle I have studied, based on precipitation with 15% sodium sulphite, is that it constitutes 10% of the total serum protein. Howe's figure is 12%. In the pig, the euglobulin fraction appears larger: the value I have found is 18%.

Of the implications of these species differences in the serum proteins for the economy of the animal it is difficult to say much. The effect on the osmotic pressure exerted by the serum of changes in the albumin-globulin ratio has been studied by several workers. Human serum was compared with horse serum by Marrack and Hewitt (1927), and the osmotic activity per gramme of protein found to vary as expected with the albumin-globulin ratio.

From the immunological point of view, the size of the globulin fraction in equine and bovine sera is sometimes a disadvantage. If a particular antibody occurs in some concentration in all the globulin fractions, "purification" of antibody by separation of a small part of the serum protein, carrying the entire activity of the serum, is obviously impossible by the conventional technique. Of course, the existence of a large globulin fraction does not preclude the possibility of the isolation of the activity in a sub-fraction such as the well-known Felton fraction in anti-pneumococcal horse serum.

These considerations apply equally well to the electrophoretic fractions. In my own experiments with the antibody to foot-and-mouth disease, in bovine serum, the antibody appeared to be associated with the γ globulin. On Svensson's estimate of 38% of the total protein for the concentration of this fraction, separation of the entire γ globulin would give only very poor concentration of antibody. This is a very different picture from the concentration of antibodies in human serum by Cohn and his co-workers, when isolation of the γ globulin gave a tenfold concentration of antibody activity.

REFERENCES

Brooksby, J., B. Unpublished Observations.
Cohn, E. J. *et al.* (1944) *J. clin. Invest.*, 23, 417.
French, M. H. (1936) *J. Comp. Path.*, 49, 118.
Hartley, P. (1914) *Mem. Dep. Agric. India. Vet.*, **1**, 178.
Hewitt, L. F. (1938) *Biochem. J.*, 32, 1540.
Howe, P. (1925) *Physiol. Rev.*, 5, 439.
Marrack, J. R., and Hewitt, L.F. (1927) *Biochem. J.*, **21**, 1127.
Svensson, H. (1946) *Ark. Kemi Min. Geol.*, 22A, 1.
Taylor, H. L., and Keys, A. (1943) *J. biol. Chem.*, **148**, 379.

The Constituents of Normal Human Blood

By C. L. OAKLEY, M.D.

THE first speaker has made it abundantly clear that the domestic animals so far examined show a remarkable variability in their blood picture. Counts of red or white cells show a variability from animal to animal seldom less than 10%, often far greater; determinations of mean corpuscular volume or mean corpuscular hæmoglobin content are equally variable. Man, by comparison, shows very little variation, and I had hitherto supposed that this was due to his large size and low metabolic rate with its consequent long cell survival time. I still think that there is a good deal of truth in this though it is very difficult on this basis to explain away the high variability of the horse. [A chart of determinations of the constituents of normal human blood was shown.]

Red cell counts and hæmoglobin determinations in man have a variability of 5 to 6% and the frequency distribution of the values obtained is a close approximation to a "normal" curve. The "orthochromic" cells form about 98% of the population, and the percentage of immature cells (reticulocytes) seldom exceeds 2%. In other words the slow replacement rate is associated with a low variability in numbers. There is a high correlation between number of red cells and hæmoglobin percentage, so that the mean corpuscular hæmoglobin concentration is fairly constant. Similarly, low variability is found in the mean corpuscular diameter (2·4%), mean corpuscular hæmoglobin (3·6%), and mean corpuscular hæmoglobin concentration (3·3%).

Two striking differences in hæmoglobin concentration may be noted. Women on the average have lower hæmoglobin concentrations than men; possibly this may be in part due to dietetic factors. Americans, on the average, have higher hæmoglobin concentrations than Britons; a fact that Price-Jones attempted to explain by supposing that Americans, who spend a high proportion of their time in motor-cars, suffer from mild chronic carbon monoxide poisoning, with consequent plethora.

It is worth noting that most domestic animals have red cell counts per c.mm. greater than that of man, while their packed cell volume is much lower; the red cell volume is therefore less than that of man. It would be interesting to consider the advantages of the small red cell in large numbers as compared with the large red cell in small numbers; questions of viscosity and rapid turnover of oxygen readily come to mind.

The counts for white cells in man have a frequency distribution differing greatly from the "normal" curve and a much higher variability than the determinations previously referred to. Indeed, it is rather doubtful whether the use of the normal curve is justifiable in dealing with the frequency distribution of a population so heterogeneous as that of white cells. White cells are short-lived and are rapidly replaced; a high variability in the white count would therefore be expected, though this might be somewhat reduced if the distributions of the individual cell types were considered separately. Like the horse, man has a high neutrophil and low lymphocyte count; in most domestic animals the proportion is reversed. True neutrophils occur, as far as I know, only in anthropoid apes and man; most so-called "polymorphs" in other animals differ greatly from human neutrophils.

Salting-out and electrophoretic methods separate the proteins in human plasma into several groups; the ones generally accepted are albumin and globulin (including fibrinogen). Electrophoretic examination divides the globulin fraction into five fractions, amounting altogether to about 40% of the total plasma protein; the remaining protein (60%) is albumin, giving an albumin-globulin ratio of 1·5. This figure is much higher than that of most domestic animals; salting-out methods give an even higher ratio.

Inherited Disorders of the Blood in Rodents

By HANS GRÜNEBERG, M.D.

THIS short paper deals only with the more important inherited blood disorders known in rodents and their main features.

Macrocytic anæmias in the mouse [1, 6, 9].—Two semi-dominant genes, W and W^{v}, are known which cause variegated spotting in the heterozygous condition ($W/+$ and $W^{v}/+$) and white fur with black eyes in the homozygotes W/W and W^{v}/W^{v} and in the compound W/W^{v}. W/W mice have a severe orthochromic macrocytic anæmia which proves fatal within a few days after birth; W/W^{v} is similarly but less severely affected and survives often until weaning age and occasionally beyond; W^{v}/W^{v} is more mildly affected, but adults are nearly always sterile; $W^{v}/+$ is mildly macrocytic; but not clinically anæmic, while $W/+$ is completely normal hæmatologically. The anæmia of W^{v}/W^{v} mice is refractory to liver treatment [6]. W/W mice can be kept alive by repeated intraperitoneal blood injections [5], but it is not certain whether this is due simply to a transfusion effect or to the presence in the normal blood of a chemical compound lacking in the anæmic mice. W^{v}/W^{v} anæmics can be acclimatized to very low atmospheric pressures like normal mice, and they show normal powers of recuperation from a superimposed secondary anæmia [6].

Siderocyte anæmia in the mouse [12, 7, 8].—The recessive gene for flexed tail and belly spot is associated with a normocytic hypochromic anæmia which develops on the 13th day of pregnancy and disappears again spontaneously during the first month after birth. The clinical anæmia is thus confined to the period of liver hæmopoiesis, while cells produced in the yolk sac or bone-marrow are normal or very nearly so. The hypochromic cells contain granules of free (non-Hb) iron. Such "siderocytes" [8] in small numbers are a normal feature of mammalian blood [2, 3]. They appear to be ageing cells about to be withdrawn from the circulation and hence are the counterpart of the juvenile cells or reticulocytes. Siderocytes are increased in numbers in all human hæmolytic conditions examined [4, 2] and their percentage affords a measure of the severity of the hæmolytic process. In practice they can be used as a very sensitive indicator for chronic lead poisoning.

Splenomegalic anæmia in the mouse [11].—A recessive condition arising before birth whose hæmatology has not yet been worked out in detail.

Acholuric jaundice in the rat [10].—The clinical condition is completely recessive, but many heterozygotes have reduced resistance of the erythrocytes to hypotonic saline and a reticulocytosis without jaundice. Homozygotes are heavily jaundiced at birth or soon after, but survive and are fertile. Microcytosis, reticulocytosis and increased fragility are associated with splenomegaly, but splenectomy does not cure the condition.

Lethal spherocytic anæmia in the rat [15].—A recessive condition which develops rapidly a few days after birth and proves fatal within a fortnight or so. The red cells are spherocytes; reticulocytes are greatly reduced in numbers, while the white count is considerably increased (mostly neutrophils). Some jaundice is present, and there are considerable hæmosiderin deposits in the liver and, to a lesser extent, under the splenic capsule. The hæmopoietic tissue in the bone-marrow is reduced. From the latter fact and the time of onset of the anæmia, it seems that the medullary hæmopoiesis is mainly (? wholly) at fault, and that its products are of an inferior quality with a reduced survival time in the circulation.

Erythroblastosis fœtalis in the rabbit [14].—No details have been published yet, but according to a personal communication it appears that the clinical picture as well as the mechanism of this disease is analogous to the human condition, depending on an antigenic incompatibility between mother and fœtus.

Pelger anomaly in the rabbit [16, 13].—A semi-dominant condition very like that described in man. In heterozygotes, which are fully viable, the nuclei of the polymorphs are either entirely unsegmented (sausage and horseshoe shapes) or consist of two segments only; normally segmented forms are rare. While the homozygous form in man is so far unknown, it has been produced in the rabbit. The nuclei of its "polymorphs" are entirely spherical. The homozygote is inviable and seems to have skeletal abnormalities in addition to its abnormal blood picture.

It will be obvious that a more detailed study of these inherited blood disorders will be of considerable interest for medical research. With the exception of the two rat genes, all the conditions mentioned above are accessible in this country.

REFERENCES

1 De Aberle, S. B. (1927) *Amer. J. Anat.*, 40, 219.
2 Case, R. A. M. (1945) *J. Path. Bact.*, 57, 271.
3 —— (1946) *Proc. roy. Soc.*, B, 133, 235.
4 Doniach, I., Grüneberg, H., and Pearson, J. E. G. (1943) *J. Path. Bact.*, 55, 23.
5 Gowen, J. W., and Gay, E. H. (1932) *Amer. Nat.*, 66, 289.
6 Grüneberg, H. (1939) *Genetics*, 24, 777.
7 —— (1942) *J. Genetics*, 43, 45.
8 —— (1942) *J. Genetics*, 44, 246.
9 —— (1942) *J. Genetics*, 43, 285.
10 Gunn, C. H. (1938) *J. Hered.*, 29, 137.
11 Hertwig, P. (1942) *Z. indukt. Abstamm.- u. VererbLehre*, 80, 220.
12 Mixter, R., and Hunt, H. R. (1933) *Genetics*, 18, 367.
13 Nachtsheim, H. (1942) *Erbarzt*, 10, 175 ; (1943) *Erbarzt*, 11, 129.
14 —— Unpublished: personal communication.
15 Smith, S. E., and Bogart, R. (1939) *Genetics*, 24, 474.
16 Undritz, E. (1939) *Schweiz. med. Wschr.*, 69, 1177 and later papers.

Professor G. R. Cameron showed a chart giving data on the blood picture, blood volume and plasma proteins of normal goats. He drew attention to the high normal level of red cell counts and hæmoglobins, pointing out that this was associated with an active red bone-marrow and small red cells in the blood. He commented on the strange reversal of albumin-globulin ratio in the plasma.

Dr. R. E. Rewell: It is surprising how little work has been done on the blood constituents of animals other than those used in laboratories or as farm animals in temperate regions.

From a hæmatological point of view, even so long-domesticated a species as the camel has been dealt with in a very superficial manner, and the best comparative study that I know is that on size and shape of the erythrocytes in several species by Gulliver in the *Proceedings of the Zoological Society of London*, as long ago as 1875. This paper even included observations on whales.

I am glad that it has been emphasized that there are marked differences between cells which are assumed to be homologous in different species. Thus in the vicuna, which I have studied recently, cells which one can only call polymorphonuclear neutrophils have granules which are finer and more acidophilic in my preparations than those of man and the average number of lobes in the nucleus is as many as fifteen. In the same animal the cells which I can only assume to be monocytes appear in first preparations to have stellate nuclei, but these are not good preparations and I have not been able yet to apply methods of supravital staining. In the few animals of this group and a few rodents which I have studied, all had smaller red cells than man.

On the biochemical side, observations appear to be even more meagre. However, Turner in America has made observations on the colloid osmotic pressure of the blood and the blood proteins in the bonito, toadfish and sea bass. In the latter animal it is of interest to note that the level could be raised by an abundant diet. Studies have, of course, been made on the blood of animals with aglomerular and atubular kidneys in connection with the elucidation of renal function.

Section of Pathology

President—A. B. Rosher, M.R.C.S., L.R.C.P., D.P.H.

[*December* 17, 1946]

DISCUSSION ON THROMBOSIS

Mr. H. J. B. Atkins: *Post-operative thrombosis.*—A limited degree of venous thrombosis is a natural response to operative trauma, but sometimes thrombosis appears at a distance from the site of the operation often in the veins of the leg. Is this a true "remote thrombosis" or is it in reality an extension from the site of the operation? Four arguments may be cited:

(1) "Thrombosis in continuity" does occur as, for instance, jugular vein thrombosis after mastoid operations and axillary vein thrombosis after radical mastectomy. However, between 1920 and 1925 at Guy's Hospital there were two cases of thrombosis of the axillary vein, one after gastrectomy and the other after prostatectomy; while of the two cases of thrombosis following radical mastectomy, both occurred in the left femoral vein.

(2) It is a fact that thrombosis of leg veins is far more common following operations in which the abdomen has been opened and it is suggested that this may be a direct spread through the inferior epigastric veins: but in the Guy's series quoted above seven cases of thrombosis followed appendicectomy by a gridiron incision, and all of these were in the left leg. If this had been a spread from the operation field, the right leg would be expected to have been the more common site. Furthermore, the increased incidence after laparotomy can be explained on the grounds that the diminished respiratory excursions consequent upon such an operation have a pronounced effect in slowing the venous return from the legs and so predispose to thrombosis.

(3) Operations upon the pelvic organs, particularly prostatectomy, have a bad reputation for leading to thrombosis of the leg veins, and it has been assumed that this is due to a direct spread from the peri-prostatic and other pelvic plexuses. Reference to the Guy's series shows that this supposedly high incidence following pelvic operations is not noticeable when the age factor is considered. Many pelvic operations, particularly prostatectomy, are performed on middle-aged and elderly patients who are naturally more prone to venous thrombosis and in fact the incidence (10 : 1,000) of thrombotic complications is as high after operations upon the stomach, duodenum and gall-bladder as upon the uterus.

(4) In a case of my own, amputation of the right leg was followed by thrombosis in the left leg without any sign of thrombosis in the stump, and in another case, the insertion of a *Kirschner* wire through the lower end of the right femur was followed by thrombosis of the left femoral vein.

well as the mechanism of this disease is analogous to the human condition, depending on an antigenic incompatibility between mother and fœtus.

Pelger anomaly in the rabbit [16, 13].—A semi-dominant condition very like that described in man. In heterozygotes, which are fully viable, the nuclei of the polymorphs are either entirely unsegmented (sausage and horseshoe shapes) or consist of two segments only; normally segmented forms are rare. While the homozygous form in man is so far unknown, it has been produced in the rabbit. The nuclei of its "polymorphs" are entirely spherical. The homozygote is inviable and seems to have skeletal abnormalities in addition to its abnormal blood picture.

It will be obvious that a more detailed study of these inherited blood disorders will be of considerable interest for medical research. With the exception of the two rat genes, all the conditions mentioned above are accessible in this country.

REFERENCES

1 DE ABERLE, S. B. (1927) *Amer. J. Anat.*, 40, 219.
2 CASE, R. A. M. (1945) *J. Path. Bact.*, 57, 271.
3 —— (1946) *Proc. roy. Soc.*, B, 133, 235.
4 DONIACH, I., GRÜNEBERG, H., and PEARSON, J. E. G. (1943) *J. Path. Bact.*, 55, 23.
5 GOWEN, J. W., and GAY, E. H. (1932) *Amer. Nat.*, 66; 289.
6 GRÜNEBERG, H. (1939) *Genetics*, 24, 777.
7 —— (1942) *J. Genetics*, 43, 45.
8 —— (1942) *J. Genetics*, 44, 246.
9 —— (1942) *J. Genetics*, 43, 285.
10 GUNN, C. H. (1938) *J. Hered.*, 29, 137.
11 HERTWIG, P. (1942) *Z. indukt. Abstamm.- u. VererbLehre*, 80, 220.
12 MIXTER, R., and HUNT, H. R. (1933) *Genetics*, 18, 367.
13 NACHTSHEIM, H. (1942) *Erbarzt*, 10, 175 ; (1943) *Erbarzt*, 11, 129.
14 —— Unpublished; personal communication.
15 SMITH, S. E., and BOGART, R. (1939) *Genetics*, 24, 474.
16 UNDRITZ, E. (1939) *Schweiz. med. Wschr.*, 69, 1177 and later papers.

Professor G. R. Cameron showed a chart giving data on the blood picture, blood volume and plasma proteins of normal goats. He drew attention to the high normal level of red cell counts and hæmoglobins, pointing out that this was associated with an active red bone-marrow and small red cells in the blood. He commented on the strange reversal of albumin-globulin ratio in the plasma.

Dr. R. E. Rewell: It is surprising how little work has been done on the blood constituents of animals other than those used in laboratories or as farm animals in temperate regions.

From a hæmatological point of view, even so long-domesticated a species as the camel has been dealt with in a very superficial manner, and the best comparative study that I know is that on size and shape of the erythrocytes in several species by Gulliver in the *Proceedings of the Zoological Society of London*, as long ago as 1875. This paper even included observations on whales.

I am glad that it has been emphasized that there are marked differences between cells which are assumed to be homologous in different species. Thus in the vicuna, which I have studied recently, cells which one can only call polymorphonuclear neutrophils have granules which are finer and more acidophilic in my preparations than those of man and the average number of lobes in the nucleus is as many as fifteen. In the same animal the cells which I can only assume to be monocytes appear in first preparations to have stellate nuclei, but these are not good preparations and I have not been able yet to apply methods of supravital staining. In the few animals of this group and a few rodents which I have studied, all had smaller red cells than man.

On the biochemical side, observations appear to be even more meagre. However, Turner in America has made observations on the colloid osmotic pressure of the blood and the blood proteins in the bonito, toadfish and sea bass. In the latter animal it is of interest to note that the level could be raised by an abundant diet. Studies have, of course, been made on the blood of animals with aglomerular and atubular kidneys in connection with the elucidation of renal function.

only the freshly formed thrombus which is liable to become detached. What we as clinicians would like to ask the pathologists is "How fresh?" In heparin and dicoumarin we have substances which will protect our patients from thrombus formation, but the former is troublesome and the latter occasionally dangerous to use, so that we wish to cut down the period of their exhibition to a minimum, and to rely as soon as we can on the natural protective mechanism of ambulation, though of course this protection is not absolute. If we knew more about the pathology of detachment we could say "after such and such a time there is no longer danger of this clot becoming detached, we may now discontinue anti-coagulant therapy and allow our patient to get up". At present we use an empirical period of two or three weeks, during which we apply our anti-coagulant therapy. This period is probably unnecessarily long and our patients are therefore subjected to unnecessary inconvenience, danger and delay. That the danger is a real one is exemplified by two cases upon whom gastrojejunostomy had been performed and who developed post-operative venous thrombosis in the leg veins. Both cases were treated by dicoumarin in comparatively small doses, both were adequately controlled by daily estimations of prothrombin time, and yet both developed severe hæmorrhages presumably from the suture line and both were only just saved by the timely administration of blood transfusions and vitamin K.

I would, therefore, conclude with the plea that, concurrently with the magnificent work that pathologists are doing in clearing up our ideas of clot formation, they should turn their attention to elucidating the problem of the pathology of detachment. In this way they will amplify and complete the great help that they are affording to the clinician in his treatment of this common and dangerous complaint.

Dr. R. H. D. Short: *Pathology of primary or idiopathic thrombosis of the leg veins.*—The causes of thrombosis are referred to changes in four fields:

Changes: (1) in the plasma; (2) in the corpuscular elements of the blood, particularly the platelets; (3) in blood flow; and (4) in the vessel walls.

A post-mortem examination of a case that has died from pulmonary embolism will illustrate their results.

The history of the patient may record an operation a week or ten days earlier from which a good recovery was made, though perhaps associated with slight pyrexia and slight pains in the calf muscles. This may have cleared up satisfactorily only to be followed by the final catastrophe. Opening the pulmonary artery, we discover the cause of death. It is a long coiled thrombus completely blocking both main branches of the pulmonary artery. Removing the thrombus and carefully disentangling its coils we find it measures about 55 cm. It may be branched particularly near one or other extremity, and towards its narrower end its colour may be much less red than is the larger portion. The paler portion is firm, almost completely inelastic and may show obvious signs of having been broken off, in contrast to the thicker end of the thrombus which is rounded. We suspect at once that the thrombus was formed in one or other femoral vein, and opening both of them we find an empty left femoral vein and the right occupied with a long thrombus. The embolism must therefore have occurred from the left femoral vein which we found empty. We also see that had the clot from the left vein been removed surgically, a second was lurking in the right femoral vein.

Let us now replace the thrombus in the position it occupied before the embolism occurred. The broken, pale end, the "kopfteil" as Aschoff would call it, fits on to the broken end projecting from the left popliteal vein. The branches near the lower

These arguments lend support to the theory that leg vein thrombosis after operation is a "remote thrombosis" and has a distinct and pathological ætiology differing from that of the physiological and insignificant "thrombosis in continuity".

Lately Gunnar Bauer (1946, *Lancet* (i), 447) has confirmed these findings by observing the early stages of clot formation in a phlebogram. He places the origin of post-operative venous thromboses in the small veins of the calf muscles whence they extend into the large venous trunks of the limb, and either obstruct the venous return and give rise to œdema, or are detached and lodge in the pulmonary arterial tree as emboli. Apart from the grave consequences of detachment, Bauer points out how a very high proportion of these cases develop late manifestations such as chronic œdema and leg ulceration if the thrombosis is allowed to develop beyond the initial stages where it must be arrested therapeutically if such tragic consequences are to be avoided. The earliest stages of thrombosis can be detected clinically by finding spots of tenderness deep in the calf muscles when the knee is flexed and the foot planted on the ground to relax these muscles; or by eliciting pain in the calf (not present on the other side) when, with the straightened knee, the ankle is forcibly dorsiflexed. Such signs call for immediate anti-coagulant therapy.

If we accept the theory of remote thrombosis the pathology of clot formation can be expressed as follows:

Intrinsic factors
(age, &c.)
+
Operation
(increased platelets and fibrinogen, recumbency, sluggish circulation)
+
? sepsis
} Tendency to thrombosis
+
Anatomical factors
(Obstruction of femoral veins especially left by loaded colon and the crossing of the left common iliac vein by the right common iliac artery)
} Thrombosis of the leg veins, especially on the left side

So much for the pathology of clot formation; what of the pathology of clot detachment? First let us consider the effect of sepsis. Whatever part sepsis may play in the formation of the clot by causing an endophlebitis, it certainly influences the possibility of clot detachment and determines what type of detachment—large or small—may take place. As a result of an analysis of the Guy's series, I envisage the effect of sepsis to be represented by the following scheme:

Thrombosis of leg veins	+	Absence of infection	=	danger of massive pulmonary embolus
	+	Mild infection	=	Anchoring of clot to vein wall by endophlebitis with œdema and pain. Portions may become detached by septic softening of the clot and lead to small infarcts
	+	Severe infection	=	Multiple septic infarcts

The use of the anti-coagulants heparin and dicoumarin has diminished the incidence of embolic manifestations following thrombosis. Now, in all probability, these substances can only act by preventing the formation of fresh thrombus and, if they have a protective effect in regard to embolus formation, it argues that it is further work showed that exactly similar hæmorrhages were found in the wall of the pulmonary artery after embolism. Here, the infarction must be the result of embolism. It cannot be due to blocking of the venous return of the vasa which empties into the bronchial veins in the case of the pulmonary artery. Vasal openings into the lumen of large veins or arteries are not, in my experience, normal and are the result either of old organized thrombosis or of arterio- or phlebo-sclerosis. These medial infarctions seem therefore to be the result of thrombosis rather than its cause.

Adherence of a formed thrombus will be favoured by all factors which stop blood flow and thus allow the vein wall to rest against the thrombus and so to increase the surface over which organization can occur. Organization proceeds rapidly and prolonged rest would seem to be unnecessary and may indeed provoke further thrombosis in what would otherwise have been healthy veins. Venous trabeculæ such as occur at the origin of the common iliac vein will act as a natural barrier to embolism.

Embolism, on the other hand, will be favoured by factors which increase blood flow and therefore increase friction on the surface of the thrombus. Increase of friction may be one factor in determining the remarkably constant length at which fracture of the thrombus occurs. Increased friability or even liquefaction of the thrombus may well be another important factor. In one case both femoral veins had originally contained thrombi extending from the inguinal ligament to below the knee. At autopsy only the upper and lower ends of the thrombi were in situ; the intervening sections had completely liquefied over a length of about one foot in both veins.

Aschoff came to the conclusion that the cause of spontaneous thrombosis lay in the blood—in its chemistry or in its hydrodynamics. In the present state of knowledge we cannot advance beyond this point though we can repeat the central problem of thrombosis which is to answer the question "why platelets deposit where they do".

Dr. Helen Wright: *Blood findings.*—The history of blood platelets goes back for nearly a century. Schultze in 1865 noticed that small granules were present in shed blood from which thin fibrils radiated during the process of coagulation. But it was not until nearly twenty years later, when the importance of these elements in thrombosis was recognized by Bizzozero (1882) and also by Eberth and Schimmelbusch (1886), that the modern experimental approach to the study of platelets can be said to have started. These workers were the first to observe that when a blood-vessel wall is damaged, a thrombus, formed of adherent platelets and white cells, becomes deposited at the site of injury to which it tends to adhere. Since then these observations have been frequently confirmed both in the human subject and in experimental animals. In this connexion the work of Rowntree and Shionoya (1927) in the United States, and of Best and his colleagues (1938) in Toronto may be mentioned.

The work of Hueck in 1926 on the part played by platelets in thrombosis was confirmed and amplified the following year by Dawbarn, Earlam and Evans (1928). All these observers found that a very marked increase in the numbers of circulating platelets followed surgical operations and parturition. This rise in count is apparent by the fifth or sixth day after operation or delivery, reaches a maximum about the tenth day and subsides to its original level again between the fourteenth and twenty-first days. The degree of the rise in numbers is correlated with the extent of tissue damage, a small superficial operation being followed by a slight rise in the platelet count, while a major operation, and especially one involving abdominal interference, end have come from the muscular veins and one large branch near the upper end evidently fits into the proximal part of the profunda femoris vein.

It is thus established that the pale end lay distally in its original position, and subsequent microscopical examination shows the typical laminated structure characteristic of the oldest part of the clot. The red portion, in many cases forming much the larger part of the thrombus, shows much less structure. Though both parts may show ripple lines of Zahn to the naked eye, these are no criteria of the age of a thrombus, which can only be settled by histological examination and by observing the platelet scaffold, which is much reduced or almost absent in the red portion. The white clot containing the platelet scaffold was therefore interpreted by Aschoff as being formed in circulating blood in contrast to the red portion, formed by massive thrombosis in a stagnant column of blood. We thus know that the oldest part of the clot lay near the knee, and the most recently formed portion lay nearest the inguinal region. The length of the clot—Aschoff says the majority are between 45 and 55 cm.—thus corresponds to the variation in the length of the femoral vein between the male and the female.

This autopsy has drawn attention to several important facts. In the first place, the clot has formed below the knee. If the distal tibial veins are opened we shall find still older, adherent, perhaps even organizing clot which can be traced into the muscular veins of the calf and even into the plantar veins. If routine examination is made of the calf veins of all cases brought to autopsy, thrombosis of these muscular tributaries is found in 22% of cases—a surprisingly high incidence. The condition may account for the transient pyrexia and calf pains noticed in the clinical history of the patient. Several surgeons, Homans in America and Bauer in Scandinavia, have drawn attention to this complication. Moreover, there are certain peculiarities about the distribution. It is found most commonly in the muscular veins to the soleus and posterior tibial muscles. The superficial, gastrocnemius muscle is usually much less affected and often escapes completely. The veins to the soleus may be widely distended with clot almost resembling varicose veins. In such cases the posterior tibial or popliteal veins may be empty and the factors which decide whether the thrombosis will spread to the larger vessels are unknown.

Routine dissection also shows that the site of thrombosis may be multiple—widely distant muscular thrombi being found with no intervening thrombosis. Or thrombosis may occur in adjacent valve sinuses with no intervening clot.

Though primary venous thrombosis is found to be so common in muscular veins of the calf and foot, it is interesting to find that there are no correspondingly common sites of thrombosis in the arms or back. Why this should be so is unknown—we may speculate upon hydrostatic factors depending on the arrangement of veins in the lower leg. Homans claims to have demonstrated histological evidence of muscular degeneration in the calf muscles which may be associated with the thrombosis. There is no proof that it is the cause. These facts are of importance in focusing attention on the primary site of thrombosis where the earliest clinical evidence may be corroborated by radiography of the veins as described by Bauer. A successful technique will demonstrate filling defects in the tibial veins and may even show the eel-like stage of thrombosis which immediately precedes a fatal embolism. In such a case, radiography may be the only clue to impending catastrophe—clinically, the stage may not be recognized.

Histological examination of the vein wall often shows an appearance of infarction of the media at the site of primary thrombosis. This observation suggests that thrombosis might be the result of interference with nutrition of the vein wall as a result of changes in the vasa vasorum. Though the idea was superficially attractive, further work showed that exactly similar hæmorrhages were found in the wall of the pulmonary artery after embolism. Here, the infarction must be the result of embolism. It cannot be due to blocking of the venous return of the vasa which empties into the bronchial veins in the case of the pulmonary artery. Vasal openings into the lumen of large veins or arteries are not, in my experience, normal and are the result either of old organized thrombosis or of arterio- or phlebo-sclerosis. These medial infarctions seem therefore to be the result of thrombosis rather than its cause.

Adherence of a formed thrombus will be favoured by all factors which stop blood flow and thus allow the vein wall to rest against the thrombus and so to increase the surface over which organization can occur. Organization proceeds rapidly and prolonged rest would seem to be unnecessary and may indeed provoke further thrombosis in what would otherwise have been healthy veins. Venous trabeculæ such as occur at the origin of the common iliac vein will act as a natural barrier to embolism.

Embolism, on the other hand, will be favoured by factors which increase blood flow and therefore increase friction on the surface of the thrombus. Increase of friction may be one factor in determining the remarkably constant length at which fracture of the thrombus occurs. Increased friability or even liquefaction of the thrombus may well be another important factor. In one case both femoral veins had originally contained thrombi extending from the inguinal ligament to below the knee. At autopsy only the upper and lower ends of the thrombi were in situ; the intervening sections had completely liquefied over a length of about one foot in both veins.

Aschoff came to the conclusion that the cause of spontaneous thrombosis lay in the blood—in its chemistry or in its hydrodynamics. In the present state of knowledge we cannot advance beyond this point though we can repeat the central problem of thrombosis which is to answer the question "why platelets deposit where they do".

Dr. Helen Wright: *Blood findings.*—The history of blood platelets goes back for nearly a century. Schultze in 1865 noticed that small granules were present in shed blood from which thin fibrils radiated during the process of coagulation. But it was not until nearly twenty years later, when the importance of these elements in thrombosis was recognized by Bizzozero (1882) and also by Eberth and Schimmelbusch (1886), that the modern experimental approach to the study of platelets can be said to have started. These workers were the first to observe that when a blood-vessel wall is damaged, a thrombus, formed of adherent platelets and white cells, becomes deposited at the site of injury to which it tends to adhere. Since then these observations have been frequently confirmed both in the human subject and in experimental animals. In this connexion the work of Rowntree and Shionoya (1927) in the United States, and of Best and his colleagues (1938) in Toronto may be mentioned.

The work of Hueck in 1926 on the part played by platelets in thrombosis was confirmed and amplified the following year by Dawbarn, Earlam and Evans (1928). All these observers found that a very marked increase in the numbers of circulating platelets followed surgical operations and parturition. This rise in count is apparent by the fifth or sixth day after operation or delivery, reaches a maximum about the tenth day and subsides to its original level again between the fourteenth and twenty-first days. The degree of the rise in numbers is correlated with the extent of tissue damage, a small superficial operation being followed by a slight rise in the platelet count, while a major operation, and especially one involving abdominal interference, elicits a rise of 100% or more. Recently I have been able to confirm these conclusions by performing graded operations in experimental animals (Wright, 1945). Other factors which affect the platelet count, such as diurnal changes, menstruation, infection and exposure to ultraviolet light are now well recognized. It has been suggested that the rise in numbers is a response to absorbed products of tissue autolysis which stimulate the megacaryocytes of the bone-marrow. The experimental injection of muscle-press juice and also of some proteins and products of protein digestion are followed by a rise in numbers though, so far as I know, no detailed chemical analysis of these materials has yet been made. Consequently no particular fraction can be incriminated as the stimulating substance for platelet formation.

But though the numbers of platelets rise after operations and their participation in the formation of white thrombi in injured vessels may be accepted as fully proven, the precipitating cause of thrombosis is still far from clear. It seemed to me, therefore, worth while to try to make quantitative observations upon the already recognized, but unmeasured property of platelets—their adhesiveness, since this characteristic seems to play so large a part in their conglutination. For this purpose, venous blood samples, treated with a minimum of heparin to ensure that no clotting took place during the course of the experiment, were introduced into special glass tubes which were carried on a large rotating wheel (Wright, 1941). The tubes containing blood were rotated at about four revolutions a minute so that it formed a thin moving layer over the surface of the glass. The tubes had windows in their sides which were closed by coverslips held in place by a thin smear of vaseline.

The windows were carefully ground so that the shoulder between the tube and the coverslip should be as small as possible, to prevent the formation of eddies at that point. The object of the window was to enable a representative section of the glass over which the blood passed during rotation to be examined microscopically at the end of the experiment. In this way the presence of adherent platelets was demonstrable in very large numbers and it may be assumed that comparatively few had disrupted during the eighty minutes of rotation. An initial platelet count was made on the sample, and I found that a direct wet method, using an ordinary red cell counting chamber and hæmocytometer pipette gave the most reliable and consistent results. Samples for counting were withdrawn every ten minutes from the rotating tubes and it was found that the count fell progressively so that, when plotted, the curves were of logarithmic type. The variation for normal bloods containing the same amounts of anti-coagulant fell within fairly narrow limits. By altering the amount of anti-coagulant, the slope of the curve can be altered. Three curves obtained from the same blood sample treated with 0·05, 0·2 and 0·8 mg. per c.c. blood respectively, demonstrated that the adhesiveness of the platelets is decreased with increasing concentrations of heparin. Even with the highest concentration of anti-coagulant, however, it is not possible to render the platelets completely non-adhesive and some continue to stick to the wall of the tube, an observation which is in agreement with the observations made *in vivo* by Shionoya and Best. Having determined the range of the stickiness of the platelets in normal subjects, I went on to make observations on patients during the post-operative period. The changes in this property were found to run parallel with the rise in their numbers. This correlation held good for surgical patients, women after delivery and in experimental animals after operations. Both the stickiness and the numbers were maximal at about the tenth day after operation or delivery.

The history of a healthy woman of 33, who underwent three spontaneous thrombotic crises following the repair of a small right femoral hernia serves to illustrate the association between thrombosis and platelet stickiness. She was under observation at the time and I was able to follow her platelet count and stickiness during the period in which they took place. Before operation both the numbers and the adhesiveness of her platelets were normal. On the seventh day after the operation, her left leg became painful and a thrombosis was diagnosed.

Her platelet count had by then increased from the pre-operative level of 240,000 to 580,000, and their stickiness was markedly increased. During the ensuing three weeks the condition subsided but at the end of this period she again complained of pain in the same leg and a further thrombosis was diagnosed. The platelet count on that day was 380,000, about the upper limit of normality, but the platelets were still unusually sticky.

Fourteen days later the platelet count had dropped to a level well below that found pre-operatively and the stickiness was returning towards normal. But that was not the end, for a week later and nine weeks after the repair of her hernia, she again developed a thrombosis. This time the platelet count was quite normal, 240,000, but an estimation of stickiness again revealed that they were abnormally adhesive. After this her convalescence was uninterrupted and she was discharged about three months after admission. In this case, therefore, all three crises appeared to coincide with phases of abnormal stickiness of the platelets.

I can offer no explanation as to why the platelets remained abnormally adhesive in this patient. Between the thromboses they returned towards normal, but never quite reached the pre-operative condition. It is also noteworthy that the count was normal at the time of the second and third thromboses, so that their initiation can hardly be ascribed to any increase in platelet numbers.

It is not yet known to what substance in their surface membrane the platelets owe their stickiness. It appears that this property is correlated with the age of the cell. Young platelets are more adhesive than are the older ones, a variation common to all young blood elements. Formerly I had inclined towards the suggestion made by Shionoya, that the platelet is covered by a thin film of fibrin, and on several theoretical grounds this explanation was satisfactory. It fitted in with their rate of migration in electrophoretic cells, with their behaviour with various types of anti-coagulant both *in vivo* and *in vitro* and with observations on their reduced stickiness in hæmophilia. Recently, however, my attention was drawn to a published case in which no trace of fibrinogen could be demonstrated in the plasma by the usual chemical tests, but in whose blood the platelets, normal in number, were reported to adhere together normally and to form white thrombi (Pinniger and Prunty, 1946). Whether it is necessary, therefore, to postulate some other mechanism than a surface fibrin film to account for the adhesive property of platelets, or whether the amount of fibrin required to render them adhesive is too small to be detected by methods used for estimating the concentration of fibrinogen in plasma, it is not yet possible to say.

Finally I should like to draw your attention to a further interesting functional change which commonly occurs in the post-operative state. It has long been suggested that circulatory stasis in the lower limbs plays a significant part in the initiation of thrombosis. Recently several workers have recorded observations made upon the rate of blood flow in the limbs after a few days' confinement to bed. Using a sodium cyanide injection method to study changes in the circulation rates after operations, Smith (1940) and her colleagues found that the time taken for blood to flow from the legs to the carotid sinus steadily increased for a number of days. Much less slowing was demonstrable in the arm to carotid sinus time during the same period so that it seems almost certain that the delay took place in the veins of the leg. How closely these changes in circulation time correspond with those in both platelet numbers and adhesiveness and how these together closely parallel the incidence of clinically diagnosed thrombosis, can be seen in fig. 1.

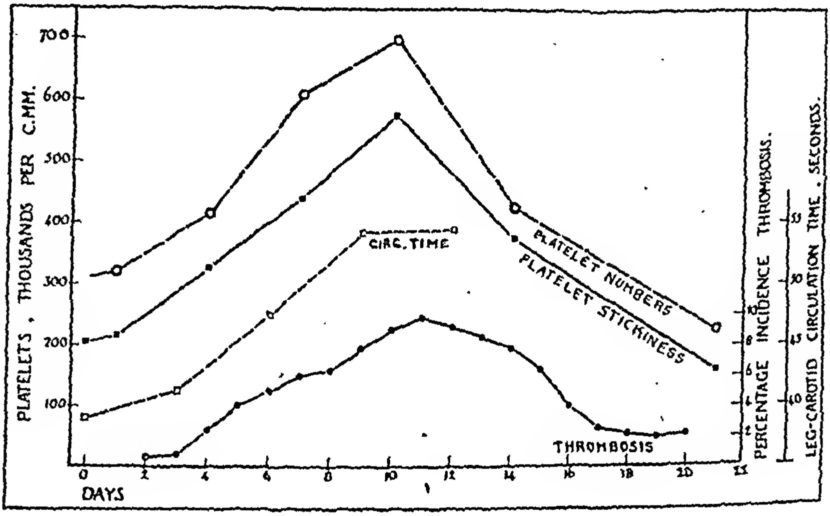


Fig. 1.

The peaks in all these curves fall suggestively near together in time and one is tempted to assume that they must be in some way causally connected and not merely coincidental. There may, of course, be some initiating or "trigger" factor capable of coming into action when other conditions in the blood are particularly favourable and whose participation in thrombosis has as yet escaped us. On the other hand all the main factors may now be known, and post-operative thrombosis takes place when all of them happen to develop high maximal values in any one patient on the same day.

REFERENCES

Best, C. H., Cowan, C., and MacLean, D. L. (1938) *J. Physiol.*, **92**, 20.
Bizzozero, J. (1882) *Arch. path. Anat.*, 90, 261.
Dawbarn, R. Y., Earlam, F., and Evans, W. H. (1928) *J. Path. Bact.*, **31**, 833.
Eberth, J. C., and Schimmelbusch, C. (1886) *Arch. path. Anat.*, **103**, 39.
Hueck, H. (1926) *Münch. med. Wschr.*, 73, 173.
Pinniger, J. L., and Prunty, F. T. G. (1946) *Brit. J. exp. Path.*, **27**, 200.
Rowntree, L. G., and Shionoya, T. (1927) *J. exp. Med.*, **44**, 7.
Schultze, C. M. (1865) *Arch. mikr. Anat.*, **1**, 1.
Smith, L. A., Allen, E. V., and Craig, W. McK. (1940) *Arch. Surg.*, **41**, 1377.
Wright, H. P. (1941) *J. Path. Bact.*, **53**, 255.
—— (1945) *J. Obstet. Gynæc.*, **52**, 253.

Section of Urology

President—R. H. O. B. Robinson, F.R.C.S.

[*November* 28, 1946]

Some Problems of Renal Lithiasis

PRESIDENT'S ADDRESS

By R. H. O. B. Robinson, F.R.C.S.

Many excellent papers on the subject of calculus in the upper urinary tract have been read before this Section. Lett (1936) described a thirty-year survey at the London Hospital which included 2,100 cases of renal and ureteric stone. He mentions the higher incidence in the male sex and the very high incidence of associated infection. In a group of 546 cases of stone in the upper urinary tract, sterile urine was found in only 12%.

Winsbury-White (1938) reported a series of cases also stressing the higher incidence in males and pointing out the preponderance of stone in the upper urinary tract as compared with the lower. He confirmed this (1946) in a further detailed statistical report.

I propose to discuss some particular problems bearing on the ætiology, diagnosis and treatment of stone in the upper urinary tract, drawing attention to several points which are still unsolved and some difficulties which I have encountered personally. The following is an illustrative case.

A young woman aged 22 in 1936 developed backache, considered to be due to spondylitis and for which treatment with heat and massage was initiated. Right-sided abdominal pain developed and two years later the appendix was removed without in any way influencing the symptoms. On interrogation she stated that all her life she had had frequency of micturition. In due course, in 1943, she was called up for service. In 1944 an attack of dysuria developed, but later in the year she proceeded to the Middle East, where a fresh attack of cystitis with hæmaturia occurred. Renal investigation, then carried out for the first time, showed bilateral renal calculi and a renal function of 48%. Retrograde pyelograms showed definite dilatation of the calices on both sides. Twelve months later the urine still contained pus but was sterile. The general condition was fair with a blood urea of 40 mg.%, but backache was persistent. X-rays at this stage showed a definite increase in the opacities, particularly in the right upper calix, and an operation was carried out to remove this upper fragment, which was discovered by preliminary needling of the kidney followed by splitting the upper pole. This was presumably done for the dilatation of the upper calix above the stone, although there was some increase in the dilatation of all the calices on both sides. Convalescence was uneventful and the post-operative X-rays showed the upper fragment removed but a definite increase in the remaining stones, while the intravenous pyelogram still showed gross dilatation particularly of the upper calix. One year later, that is to say eight years after the onset of the original symptoms, I was consulted to advise for relief of the persistent backache. The

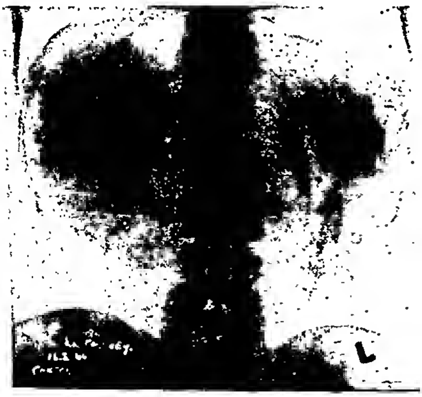


Fig. 1.—Multiple stones, both kidneys.

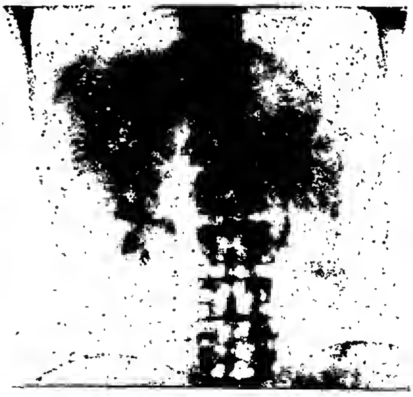


Fig. 2.—Associated dilatation of calices.

present position is that the pain is now more prominent on the left side and there is some nocturnal frequency. No obvious physical signs are present, but X-rays of the spine show bone changes of infective type. The urine is sterile but contains pus cells in fair quantity with an occasional red cell. X-rays of the kidney (fig. 1) show once more a definite shadow in the right upper calix in addition to the opacities in the lower and middle calices, and an intravenous pyelogram (fig. 2) shows the same degree of dilatation in the calices.

In this case: (1) Are we dealing with mobile renal calculi or fixed calcifications in the kidney substance? (2) Is the condition in any way associated with immobilization, the patient having been kept in bed for treatment of the spondylitis? (3) Has the kidney condition any connexion with infection, as the patient had acute cystitis, although at the time this occurred the calcification was well marked? (4) Immediately before the development of cystitis the patient was in the Middle East and therefore the possible effect of a hot climate has to be considered. In addition, she had received considerable heat treatment for her backache. (5) Lastly, can we find any indications in her case of a disordered metabolism? Under this heading are included hyperparathyroidism, hypervitaminosis D, hypovitaminosis A, toxins and maladjusted diet.

I will now discuss these various possibilities in more detail.

When I use the term mobile renal calculus, I refer to a stone which can migrate within the drainage system of the calices and renal pelvis, being of variable size but usually of such a size as to be capable of temporarily obstructing the ureter in its attempt to reach the bladder, and thereby predisposing to dilatation and stasis behind it, with an ever-present invitation to coincident infection. By fixed calcification I mean a condition which is well illustrated by the following case, which I reported to this Section in November 1934.

A woman aged 44 attended St. Thomas's Hospital in January 1934 with a three months' history of dragging pain in the left lumbar region. X-rays showed an irregular group of shadows in the lower pole. The urine was normal and cystoscopy revealed no abnormality. Pyelography showed the shadows to be in the lower pole of the kidney, outside the pelvis and without dilatation of the calices. Nine months later the patient was readmitted still complaining of pain, and it was decided to explore the kidney. There was well-marked perinephritis over the area involved, at which point the cortex was slightly depressed, yellowish in colour and gritty on section. The rest of the kidney, pelvis and ureter appeared normal. I removed the kidney on the supposition that it was tuberculous and I did not feel justified in carrying out a partial nephrectomy. Macroscopically there was a wedge-shaped area containing small calculi imbedded in the renal tissue and firmly adherent. Microscopic sections showed degeneration and chronic fibrosis of the kidney with dilatation of the tubules in the region of the calculi. Prior to operation the patient had been taking a well-balanced diet and had not had any excess of alkali. There was no evidence of disorder of the parathyroid glands, the plasma phosphate being 2·4 mg.% and the serum calcium 10·2 mg.%. Two years later, the patient was perfectly fit; but the pain was unrelieved. It is obvious that it would have been wiser to have treated the patient conservatively or performed a partial nephrectomy of the ischæmic area to avoid the potential development of renal hypertension.

Further, this type of calcification is different from that usually seen in tuberculosis, in which there is always evidence of destruction of one or more calices on pyelography and a less well-defined calcification, points discussed in detail by Sandrey before this Section in 1938. Nevertheless, Randall has recorded one very interesting case in which this type of intratubular calcification occurred outside the tuberculous area and was presumably due to the effect of the toxin on the surrounding tubules. Intratubular calcification is brought about by an excessive excretion of calcium phosphate and actual deposition in the walls of the tubules by degenerative changes in them associated with defective blood supply or toxic irritants. Experimental ligation of the renal artery and injection of mercuric chloride produce this change, as do hypovitaminosis A, hyperparathyroidism and specific toxins. The exact relationship of such calcification, Randall's Type II, to the interstitial papillary calcium plaque, Randall's Type I, is not perfectly clear, although it is conceivable that they are manifestations of the same phenomenon, that is to say, the response of the kidney to toxins, the lesion depending on the intensity, frequency and length of time the organ is subjected to their influence.

At this stage it might be well to emphasize some of Randall's findings. In investigating 1,154 autopsies he discovered subepithelial papillary calcium plaques in 19·6% and in 6·5% true renal calculi originating from plaques, that is Type I calculi. Further, in a series of 265 primary calculi voided naturally, facets of origin from a papilla were obvious in 40%. Calcium deposition occurred in a relatively avascular and devitalized area in the interstitial tissue of the papilla beneath the epithelium, sometimes being deposited in rings round the basement membrane of the collecting tubules also. No evidence of infection was present and the calcium was constantly combined in the form of calcium nucleinate and not in any other form. Subsequently the covering epithelium necrosed, exposing the plaque to urine in the calix, and a secondary deposition of calcium phosphate, calcium oxalate, or uric acid occurred. He found that his Type II intratubular calcification occurred in 1·9%, or with only a tenth of the frequency of Type I. The condition usually affected a wide area of the kidney and multiple papillæ, and in 4 of the total 23 cases true renal calculi were originating from the papillary tubular matter. In 19 cases calcium phosphate was the precipitated salt and in 4 uric acid. All grades of involvement were found and in some cases isolated intrarenal calculi. Similar examples are the uratic inspissation of infants, the calcium infarction of Henle and the nephrocalcinosis of Albright. The condition had been suspected by Huggins (1933) to be a precursor of stone and Lubarsch has pointed out that, while the calcium is usually intratubular, it may also be extratubular in the cells and especially the collagenic membrane. Infection is not a primary feature and Randall suggests that the term calcium inspissation of the collecting tubules is a better one.

Type II calculi are definitely associated with the hyperexcretory state in which the colloid crystallized balance of the urine is upset. Underlying causes are (1) supersaturation with crystalloids such as oxamide or sulphonamide, (2) hypovitaminosis A and hyperparathyroidism, and (3) urea-splitting organisms in the urine.

Decubitus calculi, recumbency stones or stones associated with immobilization develop at a rapid rate in patients who are immobilized in the supine position, and are due to stasis alone. Therefore the importance of postural drainage of the kidneys has been stressed by many writers including Ogier Ward and Boyd. Rotation of the patient on to the face for some hours during the course of the day—particularly if associated with active diuresis—drains the calices and should be carried out unless it is impossible owing to retention splints. Pulvertaft (1939) recording 60 cases, mainly of bone and joint tubercle, pointed out that this difficulty can be overcome with an anterior plaster shell. The tendency to precipitation is very much increased when calcium metabolism is upset, partly by the inevitable disuse atrophy of bone and by bone disease or bone trauma. Often an unsuitable diet with an alkaline ash base has been given and there has been insufficient stress on fluid intake. Recumbency stones are composed primarily of calcium phosphate, soft and coralline in structure and situated in the most dependent calices. They tend to disperse fairly rapidly if the kidney can be flushed by getting the patient out of bed. This type of stone is a definite problem in the traumatic surgery of war, when recumbency with bone injury is commonplace. An important feature of such calculi is that they may be extremely silent in their early stages during which they are most easily dispersed. In Boyd's paper, 3 of the 4 cases he records were associated with anterior poliomyelitis, and I have such a case under my care at the present time. Here the stasis in the kidney due to deficient respiratory movements is probably a factor. A small boy of 8 with infantile paralysis developed hæmaturia and X-ray showed multiple coralline stones in the left kidney. An I.V.P. showed these to be in the calices rather than in the cortex. Flocks (1945) pointed out the necessity for repeated X-ray investigation in recumbent cases. Examination should be carried out at intervals of one, two, three and six months after the onset of the primary condition. Higgins (1940) emphasized the need for an acid ash diet fortified if necessary by ammonium salts, pointing out that the normally acid urine becomes rapidly alkaline on immobilization. He also pointed out the undesirability of prescribing mineral oil aperients as these lead to deficient absorption of vitamin A. Injudicious and faulty instrumentation of the urethra may at any time introduce infection, and if urea-splitting organisms gain a foothold disastrous results may supervene. The failure to detect decubitus stones in their early stages has impressed me in cases of this type with which I have had to deal.

The relationship of infection to stone formation appears at first sight to resemble the fable of the hen and the egg. To simplify the problem, it is well, following Randall, to discard cases where calcification is found accompanying grossly diseased states of the kidney such as calculous pyonephrosis, chronic pyelonephritis with alkaline incrustations and simple calculi of long duration. The view is generally held to-day that at various times the kidney excretes living bacteria, that these produce changes in the renal tissue which may resolve completely, and that in the absence of obstruction chronic infection of the renal pelvis is most unlikely. The close relationship between infection and stone is brought about by the following facts: (1) Infection upsets the colloid crystalloid balance (Keyser, 1923); (2) it produces epithelial clumps which form nuclei for crystallization (Eisenstaedt, 1931); (3) it may produce papillitis (Aschoff, 1913); (4) living bacteria have been found in and cultured from the centre of calculi (Hryntschak, 1935; Hellstrom, 1936); (5) urea-splitting organisms produce calcium phosphate precipitation, as urea has definite solvent properties for this salt (Hellstrom, 1929). There is also the work of Rosenow and Meisser (1922) on specific streptococci cultured from the urine of patients with calculus, which some investigators, however, have been unable to substantiate.

Randall has carried out some extremely interesting work bearing on this point. He investigated 75 cases in which obstructing calculi were removed by open ureterolithotomy, cultures being made from the urine in the obstructed renal pelvis by preliminary aspiration. He found that in 48% the urine was sterile although ideal conditions prevailed for the growth of any organism present, while in the 52% in which the urine was infected 15 different varieties of organisms were isolated and in only 38% were staphylococci present. This conflicts with Hellstrom's postulate of at least 75% of urea-splitting staphylococci. Randall failed to find evidence of infection in his histological investigation of kidneys showing calcium plaques or intratubular inspissation. He did, however, demonstrate that the kidney is susceptible to bacterial toxins, excreting them and concentrating them in so doing. If a definite strength were reached, then the renal tissue suffered damage, the damage being most marked in the collecting tubules.

An interesting and well-substantiated observation is the fact that the organisms in the kidney urine may change from time to time; on one occasion, for example, proving to be *B. coli com.*, on another *B. lactis aerogenes* and later *B. coli* again. This suggests that the kidney urine varies considerably and that organisms absorbed from the bowel and excreted may or may not find conditions favourable to their growth, similar conditions having an opposite effect on other organisms.

The onset of tuberculosis in a kidney following preliminary obstruction by a calculus appears to be very rare, but I think this occurred in the following case:

A girl aged 5 developed tuberculous caries of the cervical spine in August 1931, and was treated by immobilization until February 1934. In May 1934 the disease became active again and further immobilization was instituted. In July 1934 transitory paraplegia developed and in November leftsided lumbar pain was complained of for the first time, but there were no urinary symptoms. The left kidney was palpable but there were no abnormal constituents in the urine. No tubercle bacilli could be found in the urine, sputum or stools. X-ray investigation showed old disease in both lungs and upper dorsal caries. The I.V.P. showed a well-developed calculus at the left ureteropelvic junction with an enlarged functionless kidney above it, whilst on the right side the kidney appeared normal in shape and function. At operation I found a phosphatic stone which I submit was of the decubitus type blocking the top of the ureter with ulcero-cavernous tuberculosis of the whole kidney, necessitating nephrectomy.

The influence of prolonged exposure to heat and sun in hot climates on the incidence of renal calculus brings out some interesting points. White races appear to have a higher susceptibility than black. Vermooten (1941), reporting on one million South African negroes admitted to hospital, found only one case of renal calculus, and the American negro, while not immune, shows a much lower incidence than the white. Pierlo and Bloom (1945) found that under desert conditions in the American Army among a group of men with adequate diet, but drinking hard water, and without pathological lesions in the genito-urinary tract, the ratio of white to coloured stone cases was 10 to 1. This upsets a dietetic causation which might operate in the African negro whose diet is deficient in calcium in spite of which the teeth and bones are perfect. Quinland (1945) investigated 16,000 hospital cases among American negroes, and found only 17 instances of stone in the upper urinary tract.

Turning now to the most important or metabolic factor in the causation of stone, we have first to consider the effect of disordered parathyroid activity. Calculi associated with hyperparathyroidism are a well-recognized group at the present time, but a point which is not so well appreciated is that they can occur without any lesions of the bony skeleton. This fact has been emphasized particularly by Albright and his associates. In a ten-year survey covering 67 cases of hyperparathyroidism they found that the typical picture of osteitis fibrosa occurred in only one-third, while in another third only mild skeletal changes were present, and in the last third no bony changes at all could be found. Albright insists that the renal changes are much more important than the osseous. Cook and Keating (1945) reported on 18 cases for the Mayo Clinic during an eighteen-month period in 1943-1944. They found that in 13 cases renal calculi were the prominent features and in the majority bone disease was minimal or absent. During the same period hyperparathyroidism was proven in 2% of all cases of renal calculus at the Clinic, but as not all calculus cases were fully investigated from this angle they consider the figure is probably higher. In many cases the stones were predominantly composed of oxalate. Foulds (1945) recorded an interesting case of bilateral renal calculi in which typical bone changes and hypophosphatæmia did not develop for eight years, although hypercalcæmia had been present for some time. In this case calcium oxalate was the predominant salt. On the experimental side Randall has produced calculi in dogs receiving parathormone and showing hypercalcæmia, finding that these calculi were of both Types I and II and that calcium deposition apart from calcium inspissation was preceded by necrotic changes in the renal tissue.

Wilder and Howell (1936) believe that there is a relationship between vitamin-D deficiency and hyperparathyroidism, vitamin D aiding in the absorption of calcium from the intestinal tract while the parathyroids mobilize it from osseous tissue.

Deficiency of vitamin A disturbs the calcium-phosphate ratio and produces changes in the epithelium of the urinary tract. Stones found under such circumstances are of Randall's Type II, starting as tubular inspissation of calcium phosphate but in prolonged hypovitaminosis severe tubular changes occur. This is probably not a very important factor at the present time in the majority of cases of stone.

The relationship of calculus in patients suffering from peptic ulcer appears well established and is readily attributable to their high intake of milk, alkalis and calcium carbonate with a resultant alkaline urine. There are, however, few statistics bearing on this particular point. Keyser (1943) stressed this fact.

Oxamide and sulphonamide calculi are obvious instances of crystallization due to the hyperexcretory state in which the colloid can no longer hold the excess crystalloid in solution.

Oxalates we have already seen are of importance as producing secondary deposition on pre-existing calcium plaques, especially if hyperoxalæmia and hyperoxaluria are present. They may occur from exogenous sources such as rhubarb or spinach, or from endogenous errors in metabolism. Oxaluria may be due to a disturbed calcium-phosphorus ratio or by incomplete oxidation of carbohydrates.

Calcium phosphorus metabolism is probably the most important factor in stone formation, as calcium figures in all the types of stone under discussion constituting the vast majority. Normal serum calcium is 9·5 to 10·5 mg.%. It is absent from the blood cells and exists as a large non-diffusible fraction combined in the serum and a small diffusible fraction in the ionized state, and varies directly with the pH of the blood, being more ionized in acid. The calcium level is influenced by parathormone, vitamin D, serum protein and the serum phosphorus, with which last it varies inversely. Hypercalcinuria is present in hyperparathyroidism, hypervitaminosis D, uræmia and many diseases of bone, the principal endogenous source of calcium: 70 to 90% is excreted in the fæces and 10 to 30% in the urine. Phosphorus normally ranges from 3 to 4 mg.% in the serum and is increased in hypoparathyroidism, hypervitaminosis D, retention nephritis and fractures. 30% of phosphorus is excreted in the fæces and 70% in the urine. Flocks investigated the relationship of stone to excessive urinary calcium excretion and found that 66% of calculus patients showed hypercalcinuria on a neutral ash diet. Normal calcium excretion is 90 to 150 mg. daily, while stone patients excreted 200 to 450 mg. on similar diet. Vitamin D and acid ash diet increase calcium elimination. An excessive chloride acidosis increases the urinary excretion of calcium and is most marked in the case of ammonium chloride, a practical point as excessive acidosis may damage the renal tubules with resultant calcification.

The metabolism of citric acid has definite relationship to the formation of renal calculi. Important contributions to this subject have been made by Scott, Huggins and Selman (1943) who pointed out that urinary citric acid runs a cyclical course with the reproductive period and that with a normal blood citrate the urinary citrate of patients with calculi was lower than normal, indicating an excessive oxidation in the kidney of citric acid in such subjects. Shorr (1945) made very interesting suggestions for the use of œstrogens and aluminium hydroxide gels in the treatment of renal stone.

Œstrogens increase the citrate excretion in the urine and lower that of the calcium. There is a definite citric acid cycle in metabolism and it is readily convertible into glycogen and glucose, participating in the oxidation of carbohydrate and fatty acids to carbon dioxide and water. Citric acid is present in large quantities in bone, where it is interrelated with calcium. The amount of urinary citric acid is regulated by, first, the urinary hydrogen-ion concentration rising in alkaline and falling in acid urine; secondly, the urinary output of calcium running *pari passu* with it; and thirdly, the sex hormones varying with the menstrual cycle, output being highest at the mid-menstrual period and lowest at menstruation. Œstrogens augment the output of citrate and androgens reduce it. The presence of the citrate-ion influences the ionization of calcium tending to replace the calcium-ion participating in the precipitation of calcium phosphate by the readily ionized soluble calcium-citrate complex, the extent of the effect depending on the relative concentration of calcium nitrate and hydrogen-ions. Below a hydrogen-ion concentration of 7 the reaction is progressively reduced, but even in acid ranges the effect of the citrate complex in removing calcium-ions is still considerable. Addition of citrate would prevent precipitation of calcium phosphate from solution, and this effect is maximal in alkaline solution in which calcium phosphate is least soluble. The effect is less in acid solution in which calcium phosphate is more soluble and requires less citric acid. This is obviously an ideal mechanism for the kidney to prevent precipitation of calcium phosphate, and it is significant that two conditions favouring precipitation, namely hypercalcinuria and an alkaline urine, are accompanied by increased excretion of citric acid. That this is a purposeful function is supported by investigating patients suffering from renal calculus. It has been shown that in many cases of recurrent renal calculi without infection subnormal amounts of citric acid and excessive amounts of calcium are present in the urine. Further, in such cases smaller amounts of orally administered citric acid are excreted than in normal controls. If infection is superadded two further unfavourable factors may arise, namely a reduction of citric acid present in the urine by the organisms which use it as a metabolite and an increased alkalinity of the urine from the organisms breaking down urea to ammonia. It is obvious that an increase in urinary citric acid excretion might prevent stone formation or check the increase of pre-existing stones. Unfortunately, feeding citric acid is useless, since however much is given by the mouth only very small increases result in the urine. If sodium citrate is given, any increase in urinary citric acid is due to increased alkalinity from the sodium-ion and is offset by the resultant reduced solubility of calcium phosphate in the alkaline urine. Œstrogens, however, increase urinary citric acid without affecting the hydrogen-ion concentration and they also lower the output of calcium. It is possible that the definitely lower incidence of renal calculus in women as opposed to men is due to this fact, the range for citric acid excretion in males lying between 0·4 and 0·7 gramme per twenty-four hours as opposed to 1·5 grammes during the mid-menstrual phase.

A further step to prevent the precipitation of calcium phosphate would be the reduction of the phosphoric-ions, and this can be brought about by administration of aluminium hydroxide gel. This forms the highly insoluble aluminium phosphate in the gut and much reduces the absorption of phosphorus. Thus the plasma phosphorus is low and with it the urinary excretion. In other words, phosphorus excretion is diverted from the kidney to the intestine. It is possible by administering aluminium hydroxide gel in amounts of 120 c.c. during twenty-four hours to reduce the urinary phosphate excretion by 90%, while still maintaining perfect calcium, phosphorus and nitrogen balance. This is especially beneficial when urea-splitting organisms are present producing highly alkaline urine with resultant diminished solubility of calcium phosphate. Acid ash diets and acidifying regimes fail when urea-splitting organisms are present, as the urine in the calices is always alkaline even if acid in the tubules. Further, renal damage is often present, which makes highly acid states dangerous. Even without infection a urinary hydrogen-ion concentration of 4·8 would be continuously necessary to dissolve a stone. Acidifying agents lower the urinary excretion of citrate and increase that of calcium, thus keeping the urine saturated and only capable of dissolving the endogenous calcium phosphate without being able to dissolve any existing calcium phosphate deposits, in other words, to inhibit further stone growth but not to remove stones already present. This helps to explain some of the disappointments in the use of stone-dissolving solutions. To summarize: Shorr suggests that it would seem probable that both œstrogens and amphojel may prove helpful in guarding against recurrent post-operative stones or the development of decubitus calculi.

TREATMENT

We can appreciate how the facts that have so far been considered have a bearing on the control of the calculus patient, particularly in the field of post-operative care. Further, that preventive treatment has to be initiated at an early stage to have any chance of success. In the case of definite renal calculi, the indications for active surgical intervention are obstruction of the drainage mechanism of the kidney either in the ureter, or renal pelvis or calices, as evidenced by dilatation shown on intravenous pyelography, with the proviso that there is no likelihood of the stone being passed naturally. Any evidence of failing function in the obstructed part or, more important, suggestion of the onset of infection, necessitates active intervention.

Non-operative treatment is indicated under the following conditions: (1) Limitation of the calculi to the cortical part of the kidney where they have no macroscopic connexion with a calix; (2) mobile stones not causing obstruction and of such a size as to make passage *per vias naturales* possible; (3) stones composed of calcium phosphate or mixed phosphatic stones; (4) bilateral stones associated with gross disease and limited function in both kidneys, rendering any operation hazardous.

Much can be done by forced fluids, by correction of faulty diet and by attempts to control superadded infection. Postural drainage may be very helpful in dislodging a stone. In the case of decubitus calculi or stones consisting wholly or largely of phosphates, attempts may be made to dissolve the calculi by the use of Suby's Solution G, and it is most important to bring this about before secondary infection supervenes, particularly with urea-splitting organisms which render the stones relatively insoluble. The continuous use of Solution G presents practical difficulties, as it necessitates the passage of a ureteric catheter over a long period of time, possibly up to two to three months, any one catheter being changed at intervals not greater than ten to fourteen days. 20 c.c. of Solution G should be injected at three-hourly intervals or some continuous irrigation apparatus used, utilizing up to 3,000 c.c. in twenty-four hours, and the desirability of using two catheters, one for inlet and one for outlet, has to be borne in mind. Sometimes dissolution will proceed satisfactorily and then be arrested owing to the stone having a part composed of some insoluble salt such as oxalate, but nevertheless it may have brought about such a reduction in size as to render the natural passage of the stone possible. Hamer (1944) recorded such a case. Another case of possible difficulty has been pointed out by Keyser. This is a slowing down or cessation of dissolution in Solution G due to the deposition of a mucoid gelatinous covering on the surface of the stone. If a 0·5% solution of urease be substituted for a few hours, this envelope is dissolved and Solution G may again prove effective.

In many cases of gross bilateral calculus disease, it is surprising how little disability the patient experiences. A patient, aged 45, had stones in both kidneys in 1933 and was operated on elsewhere. Now, in spite of gross changes he appears quite fit, has little pain and the blood urea is 43 mg.%. Obviously any operation would be extremely hazardous and could hardly improve the man's condition, while it would almost certainly render it worse.

When we return to a consideration of operative treatment, the first point that arises is the approach to the kidney, and for some fourteen years past I have favoured an incision in the line of the twelfth rib with subperiosteal resection of the rib at the posterior end of the incision. There is nothing novel in this, and I was converted to its merits by Victor Dix following the practice of Von Lichtenberg. However, I do not think its merits have been sufficiently appreciated by the majority of surgeons. Kenelm Digby recently (1941) called attention to this fact. The advantages are as follows: The incision is straight and comparatively short; it is remarkably avascular, it being quite often unnecessary to tie any vessels at all in the parietes; it is atraumatic, as it lies between the eleventh and twelfth nerves and it is as a rule unnecessary to carry the incision far forwards into the flank muscles; it gives a perfect exposure of the upper pole of the kidney, which can be explored without any undue trauma, and if necessary the suprarenal and sympathetic can also be dealt with. The pleura is far less likely to be damaged in a difficult case, and in the event of nephrectomy proving necessary it is the ideal incision. The only objection is that a second exposure of the kidney may be rendered difficult by regeneration of bone in the site of the rib.

Calculi should always be removed by pyelolithotomy if possible, and it is surprising how, with a proper exposure and suitable curved forceps to enter the calices from the pelvic incision, what a large proportion of stones can be removed in this manner. I prefer an incision in the long axis of the ureter and choose to suture the pelvic incision provided hæmostasis is complete and suture is easy, splinting the suture line with perinephric fat. On the other hand, if the pelvis is thickened and friable it is difficult and unnecessary to suture it, and I have never seen any ill-results accrue from not doing so.

Nephrolithotomy has always seemed to me an undesirable operation, and I must admit to a dread of incisions into the renal substance in order to reach an incarcerated stone. The bloodless line is a figure of speech and the suture of the kidney, even with such aids as ribbon gut and muscle or fat grafts, is not always easy. It is tempting to make the incision into the kidney with the diathermy cutting current, but this is undesirable from the long-term point of view, as it predisposes to further calcium deposition in the incised area. Even if the primary hæmorrhage is satisfactorily controlled, there is always the nightmare of secondary hæmorrhage, and it is particularly in cases where the kidney is grossly infected that nephrolithotomy is undesirable. Many of us must have had the mortifying experience of having to carry out a secondary nephrectomy in a case where a comparatively small incision has been made in the kidney substance. I have always felt that some unnecessary damage must be done to the secreting part of the kidney which is avoided in pyelolithotomy, although Mimpriss (1934) investigated this problem and could find no evidence of renal impairment after splitting the kidney. As opposed to this, Gray (1936) in experimental work on dogs found serious damage in 5 out of 12 cases.

The following case illustrates some of these points:

A woman aged 57 in 1934 had pain in the right flank, and an examination of the urine showed pus cells and *B. proteus*. A pelvic operation had been carried out many years before, and apart from a history of dental sepsis nothing was discovered in the past history. X-rays showed bilateral cortical renal calculi with a stone apparently in the upper right calix. Renal function was excellent and the blood calcium normal. Attempts were made to control the infection in the urinary tract without effect, and in 1935 (fig. 3) the small stone in the right upper calix had grown and filled the right pelvis, urine from which grew *B. proteus* on culture. I therefore removed this stone by pyelolithotomy, without any difficulty. Inadvisedly I removed the cluster of stones near the lowest calix by

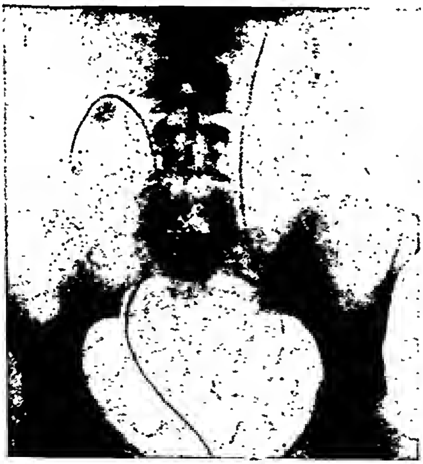


FIG. 3.—Cortical stones with large secondary stone in pelvis.

splitting the lower pole to ascertain their nature, and because I was not certain they were all fixed in the renal tissue. All seemed to be proceeding very well until the twelfth day, when she suddenly had profuse hæmorrhage into the wound and into the bladder with high fever. A transfusion and secondary nephrectomy were carried out, the kidney being offensive and necrotic in the area of the incision. Three months later the urine was reported sterile. Four years later, however, she reported with pain in the left loin and a coralline stone in the renal pelvis of the remaining kidney. Pyelolithotomy with avoidance of the cortical stones would have been wisest.

An interesting problem is whether or not to put in a nephrostomy tube after removing a renal stone, and I think on this point there is some difference between American and British practice. I consider that, in cases where dilatation has resulted from the presence of a stone, a nephrostomy tube can do no harm and may do good, and is extremely useful if lavage of the pelvis should be necessary. It is essential that drainage should be from the dependent point of the lowest calix, preferably by Cabot's method. More information is needed on the effects of nephrostomy, and I have been disappointed in the lack of recovery in the kidney which is often seen after the removal of a stone. Probably this is largely a question of the degree of infection and damage to the kidney prior to operation.

The following case is that of a man aged 27 in 1942 who had right renal colic, and in 1943 a stone was removed from the right kidney, following which operation he developed a lumbar abscess which had to be drained and he was considered unfit for further military service. He reported persistent turbidity of the urine with no other symptom. Investigation in February 1943 showed a large stone in the left kidney, with fair function and good function on the right (fig. 4). Urine was sterile but contained pus cells. Renal function was good and there was no leucocytosis. For domestic reasons operation was postponed until September 1943, during which interval he had no symptoms whatever. Operation revealed a calculous pyonephrosis and a branched stone which I removed by pyelolithotomy followed by nephrostomy and closure of the pyelolithotomy wound. Twenty-eight days later, urine from the left kidney was sterile on ureteric catheterization. Six weeks later I removed the nephrostomy tube. Seven months later he was fit, with sterile urine, but little function in the left kidney (fig. 5).

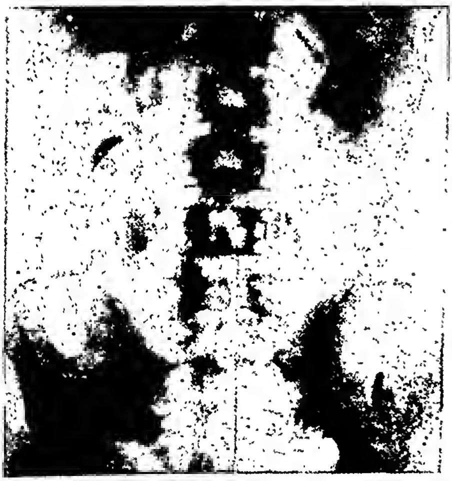


FIG. 4.—Large stone in left kidney. Good function.

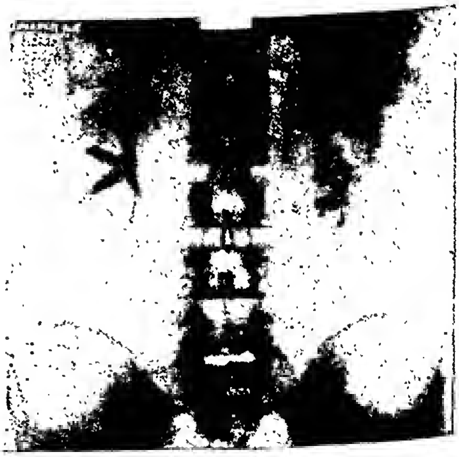


FIG. 5.—Poor function after removal of calculus.

I would emphasize again the value of a nephrostomy tube in enabling the renal pelvis to be irrigated by the two-way method with an indwelling catheter, and all evidence goes to show that this method should give the best results with stone-dissolving solutions.

I have no personal experience of the method advocated by Dees (1946) for avoiding the danger of overlooking small fragments of a branched calculus when performing a pyelolithotomy, namely by utilizing an intrapelvic coagulum of thrombin and human fibrinogen for their extraction.

The following case illustrates a more practical point in pyelolithotomy, the patient being a woman of 40 with left renal colic and hæmaturia. X-ray showed a catheter had passed easily above the stone, which was therefore unlikely to be in the ureter or ureteropelvic junction. Lateral X-ray showed the bougie in front of the stone and a pyelogram indicated a horseshoe kidney, with the stone in the lowest left calix, which was confirmed by intravenous pyelography.

In horseshoe kidney the renal pelvis lies in front and is approached in front of the renal mass in contradistinction to the usual approach from behind. I have found the operation comparatively simple if this point is borne in mind.

Calicectomy or partial nephrectomy may be used, particularly when a ragged cavity remains in the lower pole of the kidney after removal of a stone, in which case recurrence is only too likely. In a clearly incised and accurately approximated area of renal tissue, post-operative hæmorrhage is less likely than in a ragged infected cavity round a calculus.

Cases of bilateral stone require considerable judgment in deciding whether to operate at all or which side to approach first. Most surgeons are opposed to simultaneous bilateral operation, although Hryntschak reported a series of cases in which he had done so without fatality.

Nephrectomy or even nephro-ureterectomy may prove the wisest course, as the infected calculous kidney seldom if ever returns to complete normality. The presence of a dilated pelvis with residual urine in it and fibrosis in and around its walls means the inevitability of urinary infection. When, however, the disease is bilateral, conservative surgery, even if it leaves a second-rate kidney in the end, may be the only possibility. The following case illustrates this point:

A woman aged 45 complained of lumbar pain in the left side of four years' duration. She appeared a poor surgical risk with myocardial degeneration. The renal efficiency was gravely impaired and both kidneys appeared to be equally affected. The urine showed pus and triple phosphates, with a growth of enterococci on culture.

The pre-operative X-ray and the pre-operative retrograde pyelogram showed multiple stones in a dilated renal pelvis. I performed a pyelolithotomy which passed off uneventfully, and the post-operative retrograde pyelogram, two months after, showed appreciable but incomplete recovery.

URETERIC CALCULI

The indications for active surgical intervention in the case of ureteric calculus are the same as in the case of renal calculus, that is to say dilatation of the upper urinary tract above the stone, particularly if infection is superadded. If infection is present without dilatation, one should always be suspicious of further disease apart from the presenting stone in the ureter.

If neither dilatation nor infection is present, a conservative attitude can be adopted indefinitely, provided the patient is kept under close observation. Equally well, it is surprising the rate at which an obstructed kidney may become totally destroyed once infection gains a foothold. It is disturbing that these points are not better appreciated even in surgical circles, and many books of reference give an arbitrary time of six weeks for the natural passage of a ureteric calculus, which is utterly meaningless and a most dangerous doctrine.

Let me quote two cases illustrative of these points.

In March 1936 I saw a patient aged 68 who had had his right kidney removed nine years previously for calculous pyonephrosis. Three weeks prior to my seeing him he had had a brisk attack of left renal colic with some vesical irritation. He remained perfectly well with a good urinary output. X-rays showed a stone near the bladder, with good renal function. Six months later, as the stone was still present, I cystoscoped him with some misgiving, as he had a large prostate, and passed a catheter up to the kidney, alongside the stone, tying it in for forty-eight hours. There was no reaction, but it was not until six months later that the stone passed. During the whole of this time he remained perfectly fit and without any evidence of infection.

A man of 36 had a sharp attack of right renal colic, and X-ray investigation showed three stones in the lowest calix. Intravenous pyelography showed a generalized dilatation of the pelvis and calices, suggesting that the obstructing stone must have dropped back into the lowest calix. Shortly afterwards a second attack of colic developed, and unfortunately, in spite of severe and persistent pain together with fever, he was not sent up to hospital for three weeks. X-ray then showed one of the three stones impacted in the upper ureter and a complete absence of function in an enlarged kidney. When I exposed the kidney, I found it pyonephrotic and disorganized, necessitating nephrectomy.

A point of the greatest practical importance is the site of impaction of ureteric calculi, and in my experience this occurs usually either in the abdominal segment between the second and third lumbar vertebræ or on the pelvic floor in the last two inches of the ureter. Of the two the pelvic position is considerably the commoner.

The prognosis and treatment are very different in the two instances. In the case of a stone impacted in the abdominal segment of the ureter, obstruction to the secretion of urine is usually well marked and for some reason further progress seldom occurs. It is true that most of the cases seen are instances of spiculated oxalate calculi tending to imbed themselves in the ureteric mucosa, but it would appear as though there were some anatomical factor which, having once arrested the stone, makes its further progress unlikely. Some interesting observations on the relative absence of nerves in this part of the ureter have recently been made by Emerson Smith and Strasberg (1942). Spontaneous retreat of a calculus back up to the kidney is also rare, unless the stone happens to have a smooth surface, and particularly in cases where the whole ureter is dilated. Moore (1946) records such a case.

An interesting case illustrating this and other phenomena was that of a soldier aged 25, blown up in a jeep in April 1945. He was unconscious for a week, having sustained a fractured base and in addition injuries necessitating a bilateral above-knee amputation and a suprapubic cystostomy. Both stumps suppurated and his condition was critical. Two months later the suprapubic wound was allowed to heal and, although micturition was free, cystitis persisted. On November 16 he experienced left renal colic with a temperature of 103°, a palpable kidney and *B. coli* in the urine. X-rays seven days later, on November 23 (fig. 6), showed a round stone between the transverse processes of the second and third lumbar vertebræ, blocking the ureter, which is dilated above and collapsed below the stone, but demonstrates fair function in the kidney. The temperature subsided suddenly with relief of pain, and on November 26, three days later, X-ray (fig. 7) showed that the stone had retreated into the renal pelvis, appearing to have increased slightly in size. The urine now grew *B. lactis aerogenes* on culture. In view of the limb condition, no active surgical treatment was possible. On December 13 he was fit, but X-ray showed the round stone lying in the lowest calix with fair renal function but spasm of the ureter below the site of the original obstruction. On January 10, 1946, X-ray showed the same picture with improved renal function. He remained fit from the kidney point of view until March 8, when he had a further attack of left renal colic associated with fever lasting a week, the urine now growing *B. coli* again. An X-ray at this stage showed that a small oval secondary stone lay in the ureter opposite the transverse process of the

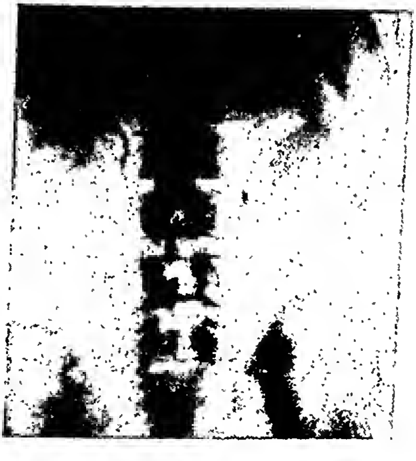


FIG. 6.—Stone in upper ureter.

fourth lumbar vertebra and that the original stone had grown considerably, partially filling the renal pelvis. An X-ray on March 22 showed some progress of the ureteric stone and fair function in the kidney without obvious dilatation. On May 7 he passed the ureteric calculus spontaneously and he has remained fit since, but X-ray on July 2 showed a well-defined branched stone which will have to be removed as soon as his general condition permits. Renal function is good on intravenous pyelography (fig. 8), but there is definite dilatation which can also be observed in some degree on the other, sound side.

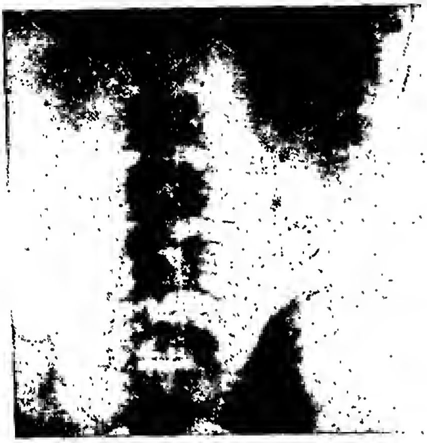


FIG. 7.—Stone passed back into renal pelvis.

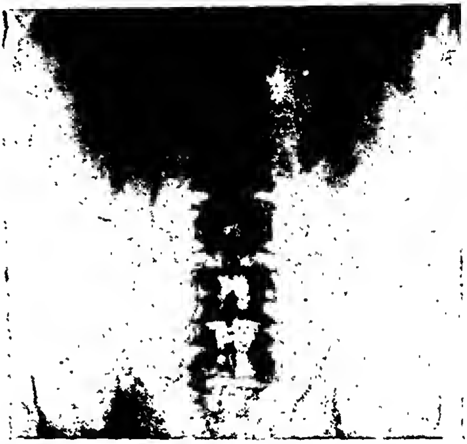


FIG. 8.—Good renal function. Large stone in left renal pelvis.

This case demonstrates first that a smooth ureteric stone can retreat into the renal pelvis, thereby relieving obstruction of the kidney; secondly, the rapid rate at which a renal calculus can grow in the presence of infection and obstruction, and the effects of continued infection on the kidney.

Retreat of a ureteric calculus may sometimes be brought about by preliminary investigations, and this fact emphasizes the importance of X-ray control immediately before or, preferably, if necessary during operation.

A woman aged 44 had left renal colic, and X-ray investigation revealed an oxalate stone blocking the top of the left ureter. A retrograde pyelogram confirmed this (fig. 9), showing a slight leak back above the stone. Some hours later, just prior to my operating upon her (fig. 10), the stone was visible in the lowest calix, from which it was easily removed by pyelolithotomy, but it might have proved difficult to find without the preliminary guide of an X-ray film.

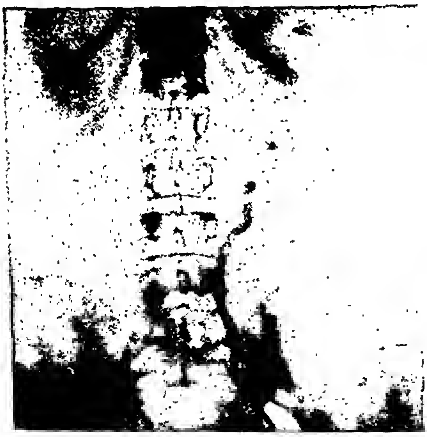


FIG. 9.—Calculus in upper ureter.

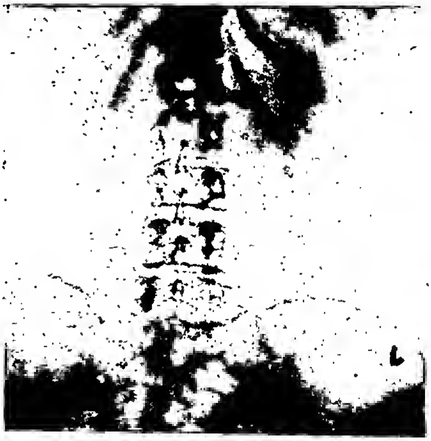


FIG. 10.—Same calculus in lowest calix.

suggesting that the obstructing stone must have dropped back into the lowest calix. Shortly afterwards a second attack of colic developed, and unfortunately, in spite of severe and persistent pain together with fever, he was not sent up to hospital for three weeks. X-ray then showed one of the three stones impacted in the upper ureter and a complete absence of function in an enlarged kidney. When I exposed the kidney, I found it pyonephrotic and disorganized, necessitating nephrectomy.

A point of the greatest practical importance is the site of impaction of ureteric calculi, and in my experience this occurs usually either in the abdominal segment between the second and third lumbar vertebræ or on the pelvic floor in the last two inches of the ureter. Of the two the pelvic position is considerably the commoner.

The prognosis and treatment are very different in the two instances. In the case of a stone impacted in the abdominal segment of the ureter, obstruction to the secretion of urine is usually well marked and for some reason further progress seldom occurs. It is true that most of the cases seen are instances of spiculated oxalate calculi tending to imbed themselves in the ureteric mucosa, but it would appear as though there were some anatomical factor which, having once arrested the stone, makes its further progress unlikely. Some interesting observations on the relative absence of nerves in this part of the ureter have recently been made by Emerson Smith and Strasberg (1942). Spontaneous retreat of a calculus back up to the kidney is also rare, unless the stone happens to have a smooth surface, and particularly in cases where the whole ureter is dilated. Moore (1946) records such a case.

An interesting case illustrating this and other phenomena was that of a soldier aged 25, blown up in a jeep in April 1945. He was unconscious for a week, having sustained a fractured base and in addition injuries necessitating a bilateral above-knee amputation and a suprapubic cystostomy. Both stumps suppurated and his condition was critical. Two months later the suprapubic wound was allowed to heal and, although micturition was free, cystitis persisted. On November 16 he experienced left renal colic with a temperature of 103°, a palpable kidney and *B. coli* in the urine. X-rays seven days later, on November 23 (fig. 6), showed a round stone between the transverse processes of the second and third lumbar vertebræ, blocking the ureter, which is dilated above and collapsed below the stone, but demonstrates fair function in the kidney. The temperature subsided suddenly with relief of pain, and on November 26, three days later, X-ray (fig. 7) showed that the stone had retreated into the renal pelvis, appearing to have increased slightly in size. The urine now grew *B. lactis aerogenes* on culture. In view of the limb condition, no active surgical treatment was possible. On December 13 he was fit, but X-ray showed the round stone lying in the lowest calix with fair renal function but spasm of the ureter below the site of the original obstruction. On January 10, 1946, X-ray showed the same picture with improved renal function. He remained fit from the kidney point of view until March 8, when he had a further attack of left renal colic associated with fever lasting a week, the urine now growing *B. coli* again. An X-ray at this stage showed that a small oval secondary stone lay in the ureter opposite the transverse process of the

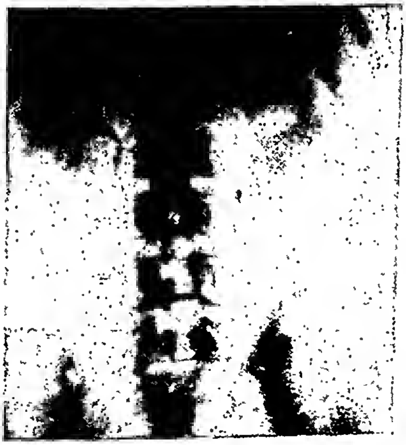


FIG. 6.—Stone in upper ureter.

for. It is surprising that it is not better appreciated that the pains associated with ureteric calculi are due to distension of an obstructed renal pelvis above and not to the onward passage of a stone, which is painless and can only occur when the ureter is relaxed. Of the instrumental methods, I have found the use of an indwelling ureteric catheter passed alongside the stone and kept in situ for forty-eight hours the most satisfactory method. If the Howard corkscrew or the Councill umbrella extractor is used, it is always wise to insert an indwelling ureteric catheter to counteract the effects of reactionary œdema. Personally I confess to being very apprehensive of their use, although I am well aware of the spectacular results that have been achieved. Wishard (1943) reported some unfortunate experiences with the basket extractor, and Dourmashkin (1945), reporting on a most exhaustive study of the cystoscopic treatment of 1,550 cases of ureteric calculus, advised against the use of forcible mechanical extraction. Councill himself (1945) recorded three instances of rupture of the ureter in a series of 504 cases. Actual meatotomy of the ureteric orifice is seldom necessary and is better avoided because of the risks of troublesome hæmorrhage and, more important, ureteric incompetence with vesicorenal reflux. If instrumentation fails, operation is called for and I have used both the mid-line and inguinal approaches. Of these the inguinal is simpler and quicker provided that the stone is not too low, in which case the mid-line approach is essential. It is accepted as axiomatic that the approach should always be extraperitoneal, but I would suggest that this is incorrect and that under certain circumstances transperitoneal approach may have great advantages, particularly in women.

On one occasion I set out to remove a stone from the lower end of the ureter by a mid-line extraperitoneal exposure, and found extreme difficulty in obtaining any adequate approach. It became obvious that a pelvic tumour was present, rendering the identification of the ureter impossible. I therefore opened the peritoneum and found a bilateral pyosalpinx, undoubtedly the underlying cause of the urinary condition, for which I carried out a bilateral salpingectomy. As a result, the ureter with the contained stone was well exposed, enabling me to open it and remove the calculus. Wishing to ensure free drainage from the kidney and to avoid extravasation of urine, I passed the fluted end of a ureteric catheter through the incision in the ureter up to the renal pelvis, subsequently passing the lower end down the ureter and through the ureteric orifice into the bladder in which the redundant part coiled up. I then sutured the ureter over the catheter and passed a stab extraperitoneal drain down to the suture line through a fresh incision in the flank. The peritoneum was then sutured over the ureter and the abdomen closed. Four days later I cystoscoped the patient and withdrew the catheter with duckbill forceps. I was so impressed with the smoothness of this patient's convalescence that I have repeated this procedure in several cases where it appeared desirable, one of which I reported in 1938.

In those cases of ureteric calculus where infection exists in the obstructed kidney behind the stone (and, according to Randall, that is in roughly 50% of cases) I have often observed a brisk flare in clinical cystitis after removal of the stone. Appreciating this fact, it is wise to culture the kidney urine and give a post-operative course of sulphonamide, if necessary.

REFERENCES

Albright, F., Sulkowitsch, H., and Bloomberg, E. (1937) *Amer. J. med. Sci.*, 193, 800.
Aschoff, L. (1913) *Path. Anat. Jena.*
Boyd, M. L. (1940) *Trans. Amer. Ass. gen.-urin. Surg.*, 33, 257.
Cook, E. N., and Keating, F. R. (1945) *J. Urol.*, 54, 525.
Councill, W. A. (1945) *J. Urol.*, 53, 534.
Dees, J. E. J. (1946) *J. Urol.*, 56, 271.
Digby, K. (1941) *Surg. Gynec. Obstet.*, 73, 84.
Dourmashkin, R. L. (1945) *J. Urol.*, 54, 245.
Eisenstaedt, J. S. (1931) *Surg. Gynec. Obstet.*, 53, 730.
Flocks, R. H. (1941) *J. Urol.*, 45, 721.
—— (1945) *J. Urol.*, 53, 427.
Foulds, G. S. (1945) *Trans. Amer. Ass. gen.-urin. Surg.*, 37, 109.
Gray, J. (1936) *Lancet* (i), 359.
Hamer, H. G., and Mertz, H. O. (1944) *J. Urol.*, 52, 475.
Hellstrom, J. (1929) *Acta chir. scand.*, 65, 545.
—— (1936) *Acta chir. scand.*, 79, Supp. 46.
Higgins, C. C. (1940) *Trans. Amer. Ass. gen.-urin. Surg.*, 33, 264.
Hryntschak, T. (1935) *Z. urol. Chir.*, 40, 211.
Huggins, C. B. (1933) *Arch. Surg.*, 27, 203.

In the case of the pelvic portion of the ureter, spontaneous passage of calculi occurs in a very high proportion of cases—in my experience 90%—although some time may be taken in the process, as in the case I quoted earlier where twelve months elapsed. Retrograde movement may occur, but usually only when hydroureter co-exists, and if planning operation this fact should be borne in mind when tilting the patient on the operating table, as it is possible to roll the stones up and down the ureter by force of gravity. In my experience the necessity for operative interference is lower among the educated sections of the community, probably because they seek medical advice at an earlier stage.

A diagnostic point of interest to be remembered is that the lower end of the ureter may lie in or very near the middle line. The original report in one case was three stones in the bladder, but on cystoscopy only one was visible, which I removed. The patient returned some months later, and subsequently X-ray showed the two remaining shadows in the bladder and considerably increased in size. They were also crushed and removed.

When we consider the actual operative technique for the removal of ureteric calculi, it can be said that in the case of calculi in the abdominal segment any form of cystoscopic removal is inadvisable and dangerous, the problem being one of open surgery. As a rule a short muscle-splitting incision below the kidney will expose the peritoneum, which is displaced forwards revealing the ureter containing the impacted stone. The ureter should be controlled above and below to prevent the possibility of the stone slipping back, and an incision made in the long axis of the ureter over the stone, which is removed. If the incision can be closed with one or two catgut sutures which approximate the edges without transgressing the lumen, I consider this ideal, although it is not essential, as provided that there is no obstruction to the ureter below, the major part of the urine will pass down into the bladder. In my experience post-operative stricture will only occur if the mucosa has been destroyed by pressure ulceration due to the calculus, in which case the kidney will usually have been rendered functionless and require removal. Some surgeons are very much opposed to suture, as they consider free drainage of the kidney essential, and if there is any doubt about the state of the ureter it is probably best to drain it with a T tube round which regeneration may take place, thereby avoiding stricture.

Obviously some œdema of the ureteric wall must occur in the early post-operative period, which may interfere with renal function and it is interesting to note what does take place.

A boy aged 12 was admitted in February 1936 with a history of right renal colic and hæmaturia three weeks previously. The pre-operative X-ray showed a small stone impacted in the abdominal segment of the right ureter with an early hydronephrosis above it, the left side being normal. I removed the stone by lumbar extraperitoneal lithotomy, suturing the ureter. Ten days after the operation, the boy had a sharp attack of abdominal pain most marked on the opposite side. X-ray now showed a considerable increase in the hydronephrosis on the operated side and a definite hydronephrosis on the sound side. The boy had no further pain and he was discharged fit and well on the fifteenth post-operative day. X-rays taken six weeks later showed both kidneys to be normal. Wells (1935) commented on the length of time taken over recovery.

When dealing with calculi in the pelvic segment of the ureter, open operation is very much a last resort. In many cases forced fluids alone suffice, and it is surprising how often cystoscopy is quickly followed by the passage of a stone. This happens so frequently that it cannot be mere coincidence, and it may be due to the dilatation of the posterior urethra leading to a reflex relaxation of the intramural part of the ureter. This occurs without the patient being aware of it, and very often the stone is voided unwittingly, which indicates how desirable it is for all urine to be passed under conditions where the expected calculus can be searched for. It is surprising that it is not better appreciated that the pains associated with ureteric calculi are due to distension of an obstructed renal pelvis above and not to the onward passage of a stone, which is painless and can only occur when the ureter is relaxed. Of the instrumental methods, I have found the use of an indwelling ureteric catheter passed alongside the stone and kept in situ for forty-eight hours the most satisfactory method. If the Howard corkscrew or the Councill umbrella extractor is used, it is always wise to insert an indwelling ureteric catheter to counteract the effects of reactionary œdema. Personally I confess to being very apprehensive of their use, although I am well aware of the spectacular results that have been achieved. Wishard (1943) reported some unfortunate experiences with the basket extractor, and Dourmashkin (1945), reporting on a most exhaustive study of the cystoscopic treatment of 1,550 cases of ureteric calculus, advised against the use of forcible mechanical extraction. Councill himself (1945) recorded three instances of rupture of the ureter in a series of 504 cases. Actual meatotomy of the ureteric orifice is seldom necessary and is better avoided because of the risks of troublesome hæmorrhage and, more important, ureteric incompetence with vesico-renal reflux. If instrumentation fails, operation is called for and I have used both the mid-line and inguinal approaches. Of these the inguinal is simpler and quicker provided that the stone is not too low, in which case the mid-line approach is essential. It is accepted as axiomatic that the approach should always be extraperitoneal, but I would suggest that this is incorrect and that under certain circumstances transperitoneal approach may have great advantages, particularly in women.

On one occasion I set out to remove a stone from the lower end of the ureter by a mid-line extraperitoneal exposure, and found extreme difficulty in obtaining any adequate approach. It became obvious that a pelvic tumour was present, rendering the identification of the ureter impossible. I therefore opened the peritoneum and found a bilateral pyosalpinx, undoubtedly the underlying cause of the urinary condition, for which I carried out a bilateral salpingectomy. As a result, the ureter with the contained stone was well exposed, enabling me to open it and remove the calculus. Wishing to ensure free drainage from the kidney and to avoid extravasation of urine, I passed the fluted end of a ureteric catheter through the incision in the ureter up to the renal pelvis, subsequently passing the lower end down the ureter and through the ureteric orifice into the bladder in which the redundant part coiled up. I then sutured the ureter over the catheter and passed a stab extraperitoneal drain down to the suture line through a fresh incision in the flank. The peritoneum was then sutured over the ureter and the abdomen closed. Four days later I cystoscoped the patient and withdrew the catheter with duckbill forceps. I was so impressed with the smoothness of this patient's convalescence that I have repeated this procedure in several cases where it appeared desirable, one of which I reported in 1938.

In those cases of ureteric calculus where infection exists in the obstructed kidney behind the stone (and, according to Randall, that is in roughly 50% of cases) I have often observed a brisk flare in clinical cystitis after removal of the stone. Appreciating this fact, it is wise to culture the kidney urine and give a post-operative course of sulphonamide, if necessary.

REFERENCES

ALBRIGHT, F., SULKOWITSCH, H., and BLOOMBERG, E. (1937) *Amer. J. med. Sci.*, 193, 800.
ASCHOFF, L. (1913) *Path. Anat. Jena.*
BOYD, M. L. (1940) *Trans. Amer. Ass. gen.-urin. Surg.*, 33, 257.
COOK, E. N., and KEATING, F. R. (1945) *J. Urol.*, 54, 525.
COUNCILL, W. A. (1945) *J. Urol.*, 53, 534.
DEES, J. E. J. (1946) *J. Urol.*, 56, 271.
DIGBY, K. (1941) *Surg. Gynec. Obstet.*, 73, 84.
DOURMASHKIN, R. L. (1945) *J. Urol.*, 54, 245.
EISENSTAEDT, J. S. (1931) *Surg. Gynec. Obstet.*, 53, 730.
FLOCKS, R. H. (1941) *J. Urol.*, 45, 721.
—— (1945) *J. Urol.*, 53, 427.
FOULDS, G. S. (1945) *Trans. Amer. Ass. gen.-urin. Surg.*, 37, 109.
GRAY, J. (1936) *Lancet* (i), 359.
HAMER, H. G., and MERTZ, H. O. (1944) *J. Urol.*, 52, 475.
HELLSTROM, J. (1929) *Acta chir. scand.*, 65, 545.
—— (1936) *Acta chir. scand.*, 79, Supp. 46.
HIGGINS, C. C. (1940) *Trans. Amer. Ass. gen.-urin. Surg.*, 33, 264.
HRYNTSCHAK, T. (1935) *Z. urol. Chir.*, 40, 211.
HUGGINS, C. B. (1933) *Arch. Surg.*, 27, 203.

KEYSER, L. D. (1923) *Arch. Surg.*, 6, 525.
—— (1943) *J. Urol.*, 50, 169.
LETT, H. (1936) *Proc. R. Soc. Med.*, 29, 1357.
MIMPRISS, T. W. (1934) *Lancet* (ii), 921.
MOORE, T. (1946) *Brit. J. Urol.*, 18, 60.
PIERLO and BLOOM (1945) *J. Urol.*, 54, 466.
PULVERTAFT, R. G. (1939) *J. Bone Jt. Surg.*, 21, 559.
QUINLAND, W. S. (1945) *J. Urol.*, 53, 791.
RANDALL, A. (1940) *Surg. Gynec. Obstet.*, 71, 209.
ROBINSON, R. H. O. B. (1934) *Proc. R. Soc. Med.*, 28, 579.
—— (1938) *St. Thom. Hosp. Rep.* (New Ser.), 3, 131.
ROSENOW and MEISSER (1922) *J. Amer. med. Ass.*, 78, 266.
SANDREY, J. (1938) *Proc. R. Soc. Med.*, 31, 749.
SCOTT, W. W., HUGGINS, C., and SELMAN, B. C. (1943) *J. Urol.*, 50, 202.
SHORR, E. (1945) *J. Urol.*, 53, 507.
SMITH, EMERSON, and STRASBERG, A. (1942) *Trans. Amer. Ass. gen.-urin. Surg.*, 35, 147.
VERMOOTEN, V. (1941) *J. Urol.*, 46, 193.
WARD, R. OGIER (1937) *Lancet* (i), 23.
WELLS, C. A. (1935) *Proc. R. Soc. Med.*, 28, 909.
WILDER and HOWELL (1936) *J. Amer. med. Ass.*, 106, 427.
WINSBURY-WHITE, H. P. (1938) *Proc. R. Soc. Med.*, 32, 163.
—— (1946) *Brit. J. Urol.*, 18, 13.
WISHARD, W. N., JR. (1943) *J. Urol.*, 50, 775.

ABSTRACT.—There are many problems concerning the ætiology, diagnosis and treatment of stone which are still unsolved. The exact relationship between Randall's type I calculus formed as a papillary plaque and therefore liable to be passed naturally at an early stage of development and the type II formed as an intratubular deposition is obscure. It is possible that they are both due to the response of the kidney to toxins, the exact lesion depending on the intensity, frequency and length of time the organ is subjected to their influence. A variety of factors contribute to stone formation, such as the hyperexcretory state with an upset of the colloid crystalloid balance in the urine, recumbency with immobilization, infection, climatic conditions and disordered metabolism. Calcium and phosphorus metabolism and their disorders are vitally concerned in calculus formation. Recent work on citric acid metabolism and its alterations due to hormonic influence point the way to efficient prophylaxis. Œstrogens increase the excretion of citrate in the urine and lower that of calcium. Addition of citrate prevents precipitation of calcium phosphate from solution, an effect which is maximal in alkaline solution in which calcium phosphate is least soluble. This is an ideal mechanism for the kidney to prevent the precipitation of calcium phosphate. Reduction of phosphate ions would enhance this effect and such reduction may be produced by the administration of aluminium hydroxide gel which forms insoluble aluminium phosphate in the gut.

Treatment of calculi may be non-operative or surgical. Obstruction and infection call for prompt surgical relief. Non-operative treatment can be advised under the following conditions: (1) Limitation of calculi to the cortical part of the kidney. (2) Mobile stones of such a size as to render natural passage possible and not causing obstruction. (3) Stones composed of calcium phosphate or mixed phosphates and therefore capable of spontaneous or therapeutic solution. (4) Bilateral stones associated with limited function and disease affecting both kidneys, rendering operation hazardous.

Forced fluids, the correction of faulty diet and the control of infection may be of great assistance. Postural drainage should be tried and in addition in the case of phosphatic stones, Suby's solution G.

When operation becomes necessary, an exposure of the kidney through an incision in the line of the twelfth rib with resection of that structure may prove extremely helpful. Pyelolithotomy is the preferable method of removing stones and in most cases this method is practicable with adequate exposure. Incisions into the cortical part of the kidney should be avoided unless absolutely essential to effect removal of a calculus. Nephrostomy is worthy of more extended trial but in unilateral cases with gross infection nephrectomy or even nephro-ureterectomy may prove the best treatment.

Most ureteric calculi are eventually voided naturally although cystoscopic manipulation may be necessary if stones are retained in the pelvic portion of the ureter. Mechanical extractors should be used with considerable caution. Operative technique should be varied to suit the individual case and illustrative cases demonstrating these points are described.

In all cases post-operative follow-up and suitable prophylaxis are most important if improvement in recurrence rate is to be brought about.

RÉSUMÉ.—Beaucoup de problèmes concernant l'étiologie, le diagnostic et le traitement de la lithiase restent à résoudre. Les relations précises entre le calcul du type I de Randall, formé comme plaque papillaire, et tendant par conséquent à être expulsé par les voies naturelles à un stage précoce de son développement, et le type II, formé comme dépot intratubulaire, sont obscures. Tous deux sont peut-être dus à une réaction du rein à l'action de toxines, la forme précise de la lésion dépendant de l'intensité, de la fréquence et de la durée de leur influence sur l'organe. Plusieurs facteurs contribuent à la formation des calculs, par exemple l'état hyperexcrétoire, accompagné d'un dérangement de l'équilibre colloïde crystalloïde de l'urine, la position couchée avec immobilisation, les infections,

les conditions météorologiques et les troubles du métabolisme. Les métabolismes du calcium et du phosphore et leurs dérangements sont de toute première importance pour la formation des calculs. Des travaux récents sur le mètabolisme de l'acide citrique et ses variations sous l'influence des hormones indiquent le chemin vers une prophylaxie effective. Les œstrogênes augmentent l'excrêtion urinaire des citrates et diminuent celle du calcium. L'addition de citrates empèche la prècipitation du phosphate de calcium d'une solution. Cet effet est au maximum en solution alcaline, où la solubilité du phosphate de calcium est au minimum. Ce mécanisme est idéal pour le rein pour empêcher la précipitation du phosphate de calcium. La réduction des ions phosphate augmenterait cet effet, et une telle réduction est possible par l'administration d'hydrate d'aluminium colloïde, qui produit du phosphate d'aluminium insoluble dans l'intestin.

Le traitement de la lithiase peut être opèratoire ou non. L'obstruction et l'infection réclament l'intervention chirurgicale prompte. Un traitement non-opératoire peut être recommandé dans les conditions suivantes: 1° Calculs limités à la partie corticale du rein, 2° Calculs mobiles de grandeur adaptée à l'expulsion par les voies naturelles, et ne produisant pas d'obstruction. 3° Calculs composés de phosphate de calcium ou d'une mélange de phosphates, et par conséquent capables d'être dissous spontanément ou par un traitement médicamenteux. 4° Calculs bilatéraux avec fonction rénale réduite et maladie atteignant les deux reins, ce qui rend l'opération dangereuse.

Les liquides forcés, la correction d'un régime défectueux et les mesures anti-infectieuses peuvent beaucoup aider. Le drainage postural doit être essayé et, en plus, dans les cas de calculs phosphatiques, la solution G de Suby.

Quand l'opération devient nécessaire, la mise à nu du rein par une incision parallèle à la 12e côte, avec résection de cet os, peut être extrêmement utile. La pyélo-lithotomie, qui est possible dans la plupart des cas si la mise à jour est suffisante, est la meilleure opération pour l'extraction des calculs. Les incisions de la partie corticale doivent être évitées à moins qu'elles ne soient absolument nécessaires pour enlever un calcul. Il vaudrait la peine de continuer les expériences de la néphrostomie, mais pour les cas unilatéraux la néphrectomie ou même la néphro-urétérectomie peut être le meilleur traitement.

La plupart des calculs urétéraux finissent par être expulsés par les voies naturelles, mais une manœuvre cystoscopique peut devenir nécessaire si les calculs sont retenus dans l'uretère pelvien. L'emploi des extracteurs mécaniques doit être accompagné de grandes précautions. La technique opératoire doit être variée selon les cas. Cet avis est illustré par la description de quelques cas.

Dans tous les cas l'observation post-opératoire et un traitement prophylactique approprié sont essentiels pour réduire la proportion de récidives.

Sumario.—Aun existen para aclarar muchos problemas de la etiologia, el diagnóstico y el tratamiento de la litiasis. Es obscura la relación exacta entre el calculo tipo I de Randall, que se forma como una placa papilar y por consiguiente es sujeto a ser evacuado por la naturaleza tempranamente en su producción, y el tipo II que se forma como un depósito intratubular. Es posible que ambos resultan de la reaccion del riñon a toxinas, la lesión exacta dependiendo de la intensidad, la frequencia y la duración del tiempo que el órgano esta expuesto a su influencia. Una variedad de factores contribuyen a la formación del calculo, como el estado hiperexcretorio acompañado por un trastorno del equilibrio coloide cristaloide en la orina, la inmovilización en cama, una infección, condiciónes climáticas y desordenes metabolicos. El metabolismo del calcio y del fósforo y sus desordenes son de primera importancia en la formacion del calculo. Estudios de origen reciente sobre el metabolismo del acido citrico y las alteraciónes que causan en este las hormonas indican el camino a una profilaxis eficaz. Los oestrogenes aumentan la excreción de citrato en la orina y disminuyen la de calcio. La añadidura de citrato impede la precipitacion de calcio fosforado de la solución, un efecto que es máximo en una solucion alcalina en laque el calcio fosforado es el minimo soluble. Esto ofrece al riñon un mecanismo ideal para prevenir la precipitación del calcio fosforado. La reducción de los iones de fosforo aumentaria este efecto y tal reducción puede ser producida por la administración del hidróxido de aluminio gel que forma en el intestino el aluminio fosforado insoluble. El tratamiento de casos de calculo puede ser terapeútico o quirúrgico. Una obstrucción o una infección exige la intervención quirúrgica inmediata. El tratamiento terapeútico es aconsejado sobre las condiciónes siguientes : (1) Cuando los calculos son limitados a la parte cortical del riñon. (2) Cuando los calculos son movibles y de tal tamaño que es possible evacuarlos naturalmente y que no causan una obstrucción. (3) Calculos del fosforado de calcio o de fosforados mezclados por esto capables de solución espontánea o terapeútica. (4) Calculos bilaterales acompañados de una limitacion de función y una condición patológica en los dos riñones, que haria arriesgada una operación.

La receta de liquidos en gran cantidad, la rectificación de alimentos defectuosos y la restricción de infecciónes pueden ser de gran ayuda. Se debe probar el drenaje postural y tambien además la solucion G de Suby en los casos con calculos fosforados.

Cuando una operación es necessaria, es muy provechoso exponer el riñon por una incisión en la linea de la costilla duodécima con resección desta estructura. Pielolitotomía es el método preferible para sacar los calculos y en la mayoría de casos este método es practicable si se emplea una exposición adecuada. Se deben evitar las incisiones en la parte cortical del riñon si no son absolutamente

esencial para sacar el calculo. Es justo probar la nefrostomia en mas casos pero en casos en que un riñon solo esta afectado y la infección es densa la nefrectomía o mismo la nefro-ureterectomia puede salir el mejor tratamiento.

La mayoría de los calculos uretericos se evacúan naturalmente con el tiempo aunque una manipulacion cistoscopica puede ser necesaria si los calculos son retenidos en el uréter pélvico. Extractores mecánicos se deben emplear con una cautela considerable. Se debe variar la técnica de operación segun cada caso individuo. Se incluyen en este estudio casos ilustrativos.

Es de primer importancia en todos los casos examinarlos de vez en cuando despues del tratamiento quirúrgico estar completo y exigir una profilaxia apropiada si una mejoría en la proporcion de reincidencias va ser efectuada.

АВСТРАКТ.—Многие проблемы, которые касаются этиологии, диагноза и лечения камней почек до сих пор еще не разрешены. Точная зависимость между первым типом камней (по Рандалю), которые образуются ввиде папиллярной бляки и потому могут быть выделены естественным путем в раннем периоде образования и вторым типом камней, которые образуются ввиде интратубулярного отложения, — вовсе не ясна. Возможно, что оба типа являются следствием влияния токсинов на почку и точное поражение почки зависит от тяжести, частоты и продолжения их действия на орган. Множество факторов предрасполагает к образованию камней, как например, гиперэкскреторное состояние с нарушением коллоидо-кристаллоидного равновесие в моче, лежачее положение с иммобилизацией, инфекция, климат или нарушенный метаболизм. Метаболизм кальция и фосфора и нарушение этого метаболизма являются весьма важным фактором в образовании камней. Самые недавние работы над метаболизмом лимонной кислоты и его изменением под влиянием гормонов, указывают на путь к успешной профилактике. Острогены увеличивают выделение цитратов в моче и уменьшают выделение кальция. Прибавление цитратов предотвращает осадок фосфата кальция из раствора, что происходит в высшей степени в щелочном растворе, в котором фосфат кальция хуже всего растворяется. Для предупреждения осадка фосфата кальция, это является идеальным механизмом для почки. Редукция фосфатных ионов увеличит этот эффект и такую редукцию можно произвести применением жела гидроокиси алюминия, который образует нерастворимый фосфат алюминия в кишках.

Лечение камней может быть нехирургическим и хирургическим. Обструкция и инфекция требуют немедленного хирургического вмешательства. Нехирургическое лечение необходимо при следующих условиях:--

(1) Присутствие камня в кортикальной части почки.
(2) Подвижные камни такого размера, что их естественный проход возможен и не произведет обструкции.
(3) Камни фосфата кальция или смешанных фосфатов с возможностью самопроизвольного или терапевтического растворения.
(4) Двухсторонние камни, связанные с ограниченной функцией и болезнь обоих почек, при которой операция слишком рискованна.

Большое количество жидкостей, исправление неправильной диэты и контроль инфекции — весьма важны. Постуральный дренаж должен быть испробован, а также раствор „G“Суби при фосфатных камнях.

Когда операция становится необходимой, обнажение почки через надрез по линии 12-го ребла с его резекцией — может быть весьма полезным. Пиэлолитотомия — более предпочтительный метод удаления камней и в большинстве случаев он возможен при достаточном обнажении почки. Нужно избегать надрезов кортикальной части почки, за исключением тех случаев, когда это необходимо для удаления камней. Нефростомия должна быть испробована более часто, но при односторонних случаях с сильной инфекцией, нефректомия или даже нефро-уретеректомия, является лучшим способом.

Большинство камней мочеточника обыкновенно выделяются естественным путем, хотя цитоскопическая манипуляция может быть нужна в тех случаях, когда камни задержаны в тазовой части мочеточника. Механические экстракторы должны быть применяемы с большой осторожностью. Операционная техника должна быть приноровлена к индивидуальным случаям. Автор здесь приводит иллюстрации для указания таких случаев.

Все больные должны быть подвергнуты наблюдению после операции. Для избежания рецидивов весьма важна соответственная профилактика.

Section of Neurology

President—Douglas McAlpine, M.D., F.R.C.P.

[*December* 12, 1946]

DISCUSSION ON THE TREATMENT AND PROGNOSIS OF TRAUMATIC PARAPLEGIA

Dr. L. Guttmann: The institution in this country of Spinal Units during the recent war was the first step forward in the systematic study of the problem of rehabilitation of spinal cord casualties, who, in the past, have been considered all too often as unemployable, useless and hopeless cripples. In this paper, a short account is given on the work carried out in the Spinal Injuries Centre, Ministry of Pensions' Hospital, Stoke Mandeville, since February 1944, on 177 casualties, out of a total number of 210 spinal cord lesions—108 were caused by gunshot injuries, 69 by fractures. 119 cases were cord lesions, the details of which are given in Table I. Of 58 cases showing cauda equina lesions, 51 involved lumbo-sacral roots and 7 sacral roots only.

The cases were admitted at varying intervals after injury, from First Aid Posts, military and E.M.S. hospitals, &c. In numerous cases, their condition was serious, owing either to the initial injury, with gaping wounds, discharging cerebrospinal fluid, or to associated injuries to other organs—in particular, lungs or extremities. In the majority of cases, the spinal lesions were complicated by contractures of the paralysed limbs. Many cases admitted at later dates showed signs of aseptic absorption with pneumonia and emaciation resulting from multiple pressure sores, urinary infection or infections of other organs. In another group of these late arrivals, where the physical condition was not unsatisfactory, the mental condition was poor. Therefore, treatment had to be very active and multifarious.

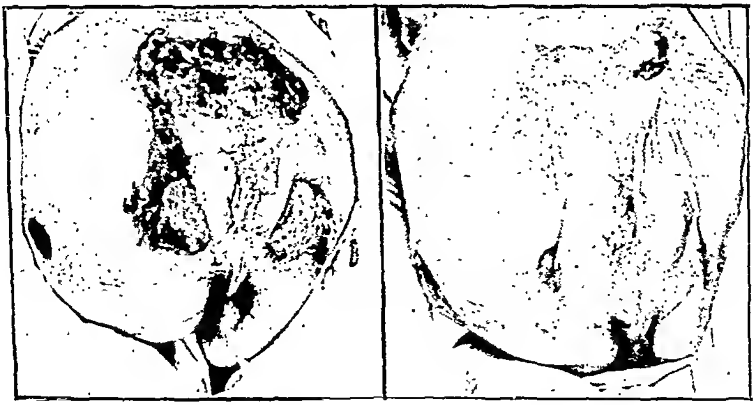


Fig. 1.

The problem of the care of the skin and the treatment of bedsores—that most serious complication which, apart from urinary infection, is the commonest cause of sepsis and death after spinal injury—has been described in detail elsewhere (Guttmann, 1945, 1946). Most of the patients arrived with multiple bedsores, some of them of gigantic and grotesque dimensions. Experience in this Centre has shown that bedsores literally as big as soup plates and exposing the bone can heal in a surprisingly short time. Fig. 1 demonstrates the stage of healing of large sacral and buttock sores four months after commencement of treatment.

Care of bladder.—Ascending urinary infection from the paralysed bladder is the other main cause of sepsis and death in spinal cord lesions and represents a problem which, in spite of all efforts and discussions on local treatment, is still unsolved. It is beyond the scope of this paper to go into details of all the various local methods which are employed to counteract urinary infection, but at least the two main procedures—namely, suprapubic cystotomy and urethral catheterization—may be evaluated. From the author's personal observations it would appear that neither urethral catheterization nor suprapubic cystotomy has yet proved a safeguard against ascending urinary infection.

Most of the cases arrived at this Centre with a suprapubic cystotomy already performed. We were, therefore, no longer in a position to decide whether any other method could have been suitably applied, for instance in incomplete lesions. As shown in Table II, suprapubic cystotomy was carried out in 148 cases, and in 112 of these within the first three days after injury. Every case with suprapubic cystotomy, whether with or without previous urethral catheterization, showed signs of urinary infection, and in a considerable number of cases the infection of the urinary tract was of severe type, including pyrexial attacks, epididymo-orchitis, stone formation in bladder, ureters and kidneys, leading to pyo- and hydronephrosis. As can be expected, the infection is introduced and maintained by the suprapubic tube, especially if the tube is left in the bladder for several weeks and has become encrusted with phosphates. Systematic and simultaneous bacteriological investigations of urine specimens and culture swabs taken from the bladder end of the catheter have repeatedly shown that the catheter contained bacteria other than those found in the urine specimen (Table III)—for instance, hæmolytic streptococci, staphylococci and *B. proteus*. The danger of transferring virulent organisms from the infected suprapubic catheter through the bladder and open ureters directly into the pelves and calices must be considerable, in view of the fact that the cystogram repeatedly revealed a reflux into ureters and kidneys in certain cases of cord and cauda equina lesions. In this connexion, it may be noted that we

TABLE I

SITE OF CORD LESIONS		Complete	Incomplete
Cervical	= 12	= 4	= 8
Upper thoracic	= 7	= 6	= 1
Mid-thoracic (T. 5-9)	= 47	= 38	= 9
Low-thoracic (T. 10-12)	= 53	= 50	= 3
TOTAL	= 119	= 98	= 21

TABLE II

SUPRAPUBIC CYSTOTOMY PERFORMED :—

On day of injury	= 34
1 day after „	= 47
2 days „ „	= 18
3 „ „ „	= 13
4 „ „ „	= 5
5–7 „ „ „	= 13
8–14 „ „ „	= 8
Over 14 „ „ „	= 10
TOTAL	= 148

TABLE III.—URINE CULTURE. (CAUDA EQUINA LESION)

Comparison of Urine Specimen and Catheter Swab

Organisms		1.3.44	13.3.44	21.3.44	Catheter 21.3.44	28.3.44	Catheter 28.3.44
Staph. pyogenes	..				+++		
Str. hæmolyticus	..						+++
Str. fæcalis	..				+++	++++	
Coliform bacilli	..	++++	++++	+		++++	
Proteus vulgaris	..				+++		+++

Organisms		3.4.44	Catheter 3.4.44	11.4.44	Catheter 11.4.44	19.4.44	Catheter 19.4.44
Staph. pyogenes	..				++		
Str. hæmolyticus	..		++				+++
Str. fæcalis	..	+++				+	
Coliform bacilli	..	+++		+++		+++	
Proteus vulgaris	..		++		++		+++

have encountered several cases where frequent pyrexial attacks, due to urinary infection, ceased when the suprapubic drainage was discontinued.

In cases of middle or upper thoracic lesions the bladder was found extremely contracted. Moreover, once the uninhibited automatic function of the bladder has developed, suprapubic cystotomy does not prevent reflex detrusor action of the infected urine through the urethra and thus does not prevent the development of epididymo-orchitis. These facts show that there is no reason to consider suprapubic cystotomy as *the method of choice* in the treatment of every case of paralysed bladder. Judging from war experience, it has proved valuable only as an emergency measure on the battle-field, when immediate transfer of spinal injuries to adequate hospitals was impossible. Under peacetime conditions, the prompt transfer of a paraplegic to a Spinal Centre should be practicable in almost every case, and this appears to be the best guarantee for a more specialized treatment of the paralysed bladder. There are instances in which suprapubic drainage is indicated and is even preferable to urethral drainage as the lesser evil of the two—in particular, in cases with narrow urethra, urethral strictures and other local urethral injury, and in some with special nursing problems. Further experience will show whether Riches' special method of suprapubic catheterization (1943) is preferable to the open suprapubic cystotomy.

Tidal drainage has proved a valuable auxiliary method in a number of our cases, especially in the early stages after cord and cauda equina lesions, in cases both with suprapubic drainage and indwelling urethral catheter. This may be emphasized, in view of the fact that, during the last two years, the enthusiasm for this method, as instigated by Munro, 1936, has somewhat waned. This method was found of special value for removing mucus and small stones from the bladder, the latter especially from the posterior wall, if the patient is placed in prone position. However, it must be admitted that this method is of use only if it is understood by everyone concerned, including the patient, and is constantly supervised. In certain cases of small bladders, with uninhibited detrusor activity, in cord lesions, and also in some cases of cauda equina lesions with rigid bladder walls, tidal drainage has not worked satisfactorily, in spite of all efforts. The apparatus used in this Centre is that designed by Riches (1943), which has the advantage of being equipped with a manometer and can be used for cystometrograms. The fluids used for irrigation are ½% acetic acid, 4% boric acid and flavazole 1 : 2,000. In cases with stone formation, we have used solution G (Suby, Suby and Albright, 1942). However, our experience with this solution has proved less satisfactory, and from the rehabilitation point of view the author prefers instrumental removal of calculi from the urinary tract by a skilled urologist, as this is the safest and quickest method of removal. Once calculi are removed, we carry on with solution G for a certain period.

The development of automatic reflex activity of the bladder wall in spinal cord lesions and voluntary micturition by pressure of the abdominal wall in lower cord and cauda equina lesions are encouraged and exercised, as recommended in the Great War by Riddoch (1918). Whenever practicable, suprapubic drainage is discontinued. This has so far been carried out in 94 cases out of 148 at various intervals. Healing of the suprapubic wound is often delayed by the profound fibrosis of the suprapubic tract, and even surgical closure by excision of the tract and resuture does not always prevent the breaking down of the tract, especially in cases with low suprapubic cystotomy and those in which suprapubic drainage was discontinued at later dates. When suprapubic drainage is discontinued, it is necessary, especially during the first period after discontinuation, to continue bladder washouts intermittently by urethral catheterization at various intervals, or by temporary drainage with an indwelling catheter of small size. By this procedure, we have even succeeded in rendering the urine, infected by suprapubic cystotomy, sterile in a few cases. In this Centre, intermittent urethral catheterization and continuous catheterization, the latter if combined with tidal drainage, and with change of indwelling catheter every two to four days, have proved satisfactory. In cases in which urethritis develops, the bladder washout has to be combined with washouts of the urethra itself with flavazole solution 1:2,000. Paraplegics with long narrow foreskins tend to develop balanitis, and it is better in these cases to carry out circumcision, or at least a dorsal slit, as soon as possible.

Pyrexial attacks, due to urinary infections, are counteracted by courses of sulphonamides and systemic courses of penicillin.

Whatever local methods in the treatment of paralysed bladders are used, two of the main factors in the treatment, in particular for prevention of stone formation, are the *shortening of the duration of the recumbent position and the restoring of the best possible physical fitness of the man.* The former is more feasible in cases of gunshot injury and fractures of transverse and spinous processes with spinal cord involvement, as the support of the spine has not been interfered with in the majority of cases.

EFFECTS OF BLADDER DISTENSION ON AUTONOMIC MECHANISMS.

In connexion with the care and treatment of the bladder after spinal cord injuries, certain reflex reactions in the autonomic nervous system must be mentioned, which are set up by distension of the bladder (and this applies also to rectum and colon) due to any cause, as these phenomena are not only of interest from a theoretical point of view, but have practical importance. Some of these phenomena have been previously observed: they have, for instance, been mentioned in Head and Riddoch's classical study on mass reflexes (1917), and in more recent years studied experimentally by Carmichael *et al.* (1939).

During studies on sweating, in relation to bladder distension in spinal cord lesions, my attention was drawn to various other reflex responses. Several patients with complete upper thoracic lesions, on distension of the bladder, which did not give rise to any sensation of pain below the level of the lesion, developed patchy flushing of face and neck, profuse localized sweating over head and shoulders or at the level of the lesion, blockage of nasal air passage and nasal voice, a slow pulse with occasional extrasystoles, respiratory discomfort, and fullness in the head, which progressed to severe occipital or frontal headaches. It was at once realized that this was a phenomenon of autonomic mechanisms, in which a stimulus arising from a distended viscus below the level of a complete spinal cord lesion effected, along extramedullary pathways, profound disturbances of the cardiovascular activity in parts of the body above the level of the lesion. In order to investigate and record all the details involved in this reflex phenomenon, a research team was organized with Dr. Whitteridge and his colleagues from the Physiological Department, Oxford, and we examined vasomotor response and heat regulation by measuring skin temperatures below and above the level of the lesion, in relation to rectal temperature, sweating, blood-pressure, pulse volume and blood-flow, pulse-rate, respiration, and conscious sensation. It was found that these reflex responses were dependent in consistency and intensity on the level of the lesion. They were most conspicuous in all complete lesions of the cervical and upper thoracic cord down to T. 5—in other words, in those lesions in which the greater part of the splanchnic control was crippled. In such cases, the rise of blood-pressure due to bladder distension was high, and values of 190-260 mm.Hg of systolic and 125 to 135 mm.Hg of diastolic blood-pressure were recorded. Further details will be given in Dr. Whitteridge's report and a full description of our work will be published shortly elsewhere.

From a practical point of view, knowledge of these reflex responses above the level of a cord lesion is important, as they indicate abnormal activity of a viscus in the anæsthetic area below the level of the lesion. They can be diagnosed simply from facial appearance, and their recognition by medical and nursing staff will be a guide for immediate and correct action. Moreover, they explain why complaints of headaches and fullness in the head in paraplegics have always to be considered seriously, as they may be a warning of impending abdominal catastrophe.

PHYSICAL REHABILITATION

Physiotherapy in paraplegics, to be effective for restoring the man's fitness to the highest possible degree for independence, working capacity and family life, must be applied early and practised persistently. The aims of physiotherapy can be divided into two main groups:

(1) *Prevention of contractures and atrophy and treatment of the various forms of spasms.*—The methods employed include keeping the limbs in the correct position, passive movements, bath therapy, and surgical procedures. Permanent fixation of paralysed limbs in any position is discouraged. The most deleterious type of contractures was found in cases admitted in plaster beds, in which patients had lain for months. Not only have plaster beds proved no better method for preventing and healing sores, for which they were previously advocated, but they have actually promoted the development of sores. Moreover, the contractures of the joints and the atrophy of the tissue of the back, caused by this type of fixation, were profound, and it took a very long time to remedy the damage done. Therefore, plaster beds must be condemned as being contrary to the fundamentals of rehabilitation in paraplegics.

In relation to the prevention and treatment of flexor spasms, the importance of the various intrinsic and extrinsic factors in lowering the threshold of reflex activity of the part of the spinal cord below the level of the lesion may be emphasized. Distension of bladder, colon and rectum, and the irritation of sensory organs in contracted joints and tendons are violent initiators of reflex spasms. Regular passive movements have proved most beneficial in the treatment of spasms. Even extreme degrees of flexor spasms and contractures may be greatly improved by this conservative method, especially if the passive movements are carried out in a continuous bath. The importance of standing exercises in parallel bars for the relaxation of spasms, apparently by setting up inhibitory impulses to the unrestrained activity of the flexor groups, may also be mentioned here.

Surgical measures for the treatment of spasms, especially anterior root sections, should be restricted to selected cases. In such cases, intramedullary alcohol injections—1 to 2 c.c. of 80% alcohol—into the thoraco-lumbar junction of the cord, using a fine needle, may be tried first, as being the less arduous method. The immediate effect of such an injection in abolishing the most violent flexor spasms can be very striking, as shown in a case of complete lesion at T. 10 (fig. 2). However, the first injections had only a temporary effect in our three cases, and further injections had to be given, in order to produce a more lasting effect. Further experience with this method will be published in the near future.

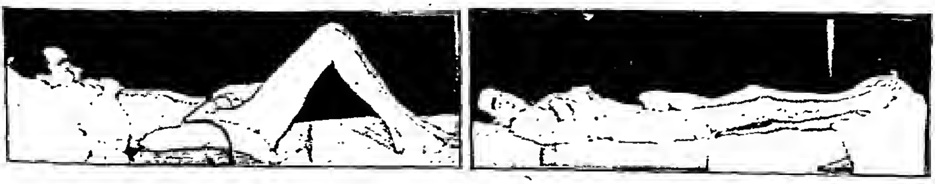


FIG. 2.—Effect of intramedullary alcohol injection into the thoraco-lumbar junction of the cord, in a patient with a transverse lesion at T. 10 and violent flexor spasms.

(2) *Adaptation therapy of normal parts of the body by compensatory training.*—Exercises of normal parts of the body are carried out with a view to readjustment of the vasomotor control to postural changes and to the over-development of those muscles which are essential for the patient's upright position, as well as those which have a synergic function in relation to the paralysed muscles and can compensate for their loss. Details of the technique of compensatory training, in which sling and spring exercises, dressing, balancing, walking exercises and games, adapted to the paraplegic's limited abilities, have proved invaluable, have been published elsewhere (Guttmann, 1946). We have found, in confirmation of previous experimental work (Hill and Barnard, 1897 and others) that gravity has a profound effect upon the blood circulation, especially blood-pressure, in cases of high thoracic and cervical lesions, in which the vasomotor control is crippled. Such a patient, when raised to the upright position, will tolerate this position badly. However, if well trained, he develops postural adaptation mechanisms, which may be regulated by carotid sinus and other blood collectors to act as "emergency adaptors".

PREVOCATIONAL TRAINING AND RESETTLEMENT

Along with physical readjustment goes rehabilitation by work. This is started with occupational therapy in the form of simple handicrafts, whilst the patients are confined to bed because of sores and urinary infection. This therapy is not merely occupation as a diversional measure—it is invaluable for the development of the dexterity of the fingers and arms, upon which the future vocation of a paraplegic will depend. As soon as possible, prevocational training is added. It includes leather-work, precision engineering, clock assembly, shoe repair, carpentry, typing and shorthand, and correspondence courses in various trades. This work is graded and correlated to the physical improvement of the man and to his previous personality. The benches and tools in the workshops are adjusted to the individual patient's disability. Most of the men have shown keen interest in prevocational training, either to readjust their former trades to their permanent disability or to take up training in a new occupation. Indeed, early vocational training in hospital has proved to be most useful as a step forwards in the social rehabilitation of paraplegics and has restored activity of mind.

In relation to domestic and industrial resettlement, one has to distinguish between two groups of paraplegics. The first group consists of those patients who will not be able to return to their homes. For these men, permanent settlements adapted to their disabilities will be established, in which married and unmarried patients can live in sheltered conditions and from which they can go out in their wheel chairs to their places of employment. Those who are not able to go out to work will have an opportunity of doing work which will be adjusted to their disabilities in the settlements. The first of such settlements, which has been opened recently with patients from this Centre, is situated near Macclesfield and is run by the British Red Cross Organization.

Another group of patients will be able, and will prefer, to return to their homes, if these can be adjusted to their disabilities, or if special bungalows can be built for them. The British Legion is already co-operating in this work. 48 out of 84 patients discharged from this Centre have returned to their homes, and 29 of these are working. 36 patients were transferred to special convalescent homes set up at Chaseley, Eastbourne, and the Star and Garter Home, Richmond, pending their admission to permanent settlements or training centres, or return to their own homes.

It is at present rather premature to make definite statements about the ultimate survival period of paraplegics of the recent war. However, judging from our own cases, it has been proved that at least the early mortality after spinal cord injury is much lower than one would expect from the statistics of World War I. In our statistics of 164 survivors out of 177 cases (Table IV), all but 2 were cases from

TABLE IV

SURVIVAL AFTER INJURY	
Under 1 year	= 4
1 ,,	= 3
1½ years	= 24
2 ,,	= 35
2½ ,,	= 53
3 ,,	= 24
4 years	= 10
5 ,,	= 3
6 ,,	= 5
7 ,,	= 1
Over 7 ,,	= 2
TOTAL	= 164

DEATH AFTER INJURY	
Within 1st year after injury	= 8 (4 within 1st 6 mths.)
2nd ,, ,, ,,	= 1
3 years ,, ,,	= 2
4½ ,, ,, ,,	= 1
5½ ,, ,, ,,	= 1
TOTAL	= 13

the recent war. It should be noted that our low mortality statistics include 3 cases in which death was obviously caused by injuries and pathological process of other organs (lungs in 2 cases, heart in 1 case).

In conclusion, it can be said that the results achieved in the rehabilitation of paraplegics are very encouraging, in so far as the medical problem is concerned. However, there is much more to be done for their social and industrial rehabilitation. In particular, there is still great need to adjust the attitude of the public towards the permanent disability of paraplegics. Any condition which maintains or induces a sense of inferiority should be avoided. These men do not look for charity but for understanding assistance in their efforts to master their disability and adjust themselves to life again. "Adjust or perish"—that fundamental principle in the universe, which enables the weaker to master life and to compete successfully with the stronger, can be applied in its full meaning to the rehabilitation of paraplegics.

REFERENCES

CARMICHAEL, E. A., DOUPE, J., HARPER, A. A., MCSWINEY, B. A. (1939) *J. Physiol.*, 95, 276.
GUTTMANN, L. (1945) *Med. Times, N.Y.*, 73, 318.
—— (1946) *Brit. Phys. Med.*, 9, 130, 162.
HEAD, H., and RIDDOCH, G. (1917) *Brain*, 40, 188.
HILL, L., and BARNARD, H. (1897) *J. Physiol.*, 21, 323.
RICHES, E. W. (1943) *Brit. J. Surg.*, 31, 135.
RIDDOCH, G. (1918) *Lancet* (ii), 839.
SUBY, H. I., SUBY, R. M., and ALBRIGHT, F. (1942) *J. Urol.*, 48, 549.

Mr. E. W. Riches: I propose to confine my remarks to the treatment of the urinary tract.

A lesion producing complete interruption of the spinal cord or cauda equina causes paralysis of the bladder; the stages through which this viscus passes are essentially the same for all injuries causing paraplegia. They are (1) complete retention; (2) retention with overflow or passive incontinence; (3) periodic reflex micturition. After incomplete or transient interruption a state of voluntary micturition differing little from the normal may ensue.

The aim of treatment is to leave the urinary tract free from infection, with a bladder of adequate capacity from which urine can be passed without incontinence, preferably by the natural passage. The initial treatment of the bladder is of great importance; if it is correct it may well suffice as the line of treatment throughout; if it is wrong it may condemn the patient to urinary sepsis and early death.

The first essential is to drain the bladder; this does not mean that drainage must be carried out immediately. The former teaching that the bladder should be emptied by catheter as soon as possible after the injury is harmful. The bladder should be allowed to distend, and this will usually take at least twenty-four hours and often more. It can safely be left for thirty-six or forty-eight hours without being emptied if it is not infected. It will not rupture, it will overflow, and distension for two days will not produce such impairment of function as to preclude ultimate complete recovery. The recognition of this fact obviates the need for immediate drainage and allows time for the patient to be moved to suitable surgical surroundings. Failure to recognize it often leads to urethral catheterization under poor conditions, and serious infection follows in almost every case when urethral catheterization is continued for more than two days. It is true that there are rare cases in which the retention is painful, and if the pain is not relieved by morphia it is then permissible to empty the bladder by aspiration through a serum needle inserted well above the pubes. This may if necessary be repeated once, but frequent aspiration is likely to lead to extravasation. Under peacetime conditions however it should rarely be impossible to get the patient into hospital within twenty-four hours; during the war mobile teams often made surgical treatment available in a shorter time.

Let us then assume that twenty-four hours have elapsed, the bladder is distended, there has been no voluntary or automatic micturition and the surroundings are such that reasonable asepsis is possible. Is the bladder to be drained by urethral or suprapubic catheter? I may say at once that I strongly advocate the suprapubic route for general use. It is true that we have had one or two cases received into the Spinal Injuries Centre at Stoke Mandeville very soon after their injury where the urethral catheter combined with tidal drainage and adjuvant measures have been used successfully, but they form a very small minority. They require infinite care and unlimited time, and their supervision is a one-man job. Incidentally paraplegics should never be catheterized by an orderly. When drainage is established it must be adequate and regular or continuous; it must be such as to prevent extreme contraction or excessive dilatation of the bladder, there must be no urinary leakage, and above all it must avoid the possibility of serious infection. The method must be one which the nursing staff can understand and care for. The method I advocate is the introduction of a small suprapubic catheter into the upper part of the distended bladder. Its track must be oblique, and the catheter must fit closely. I do not refer to suprapubic cystotomy as usually performed. We all have often been horrified by the large tube placed at the bottom of a long incision with urine leaking around it and infection getting in. At a later stage the track becomes adherent to the pubes and closure is at best delayed and at worst impossible. Moreover the bladder is allowed to contract down to a small capacity, and any periodic reflex micturition which may ultimately develop is useless because of its frequency. Examples have been shown previously (Riches, 1944).

I have described elsewhere the method of suprapubic catheterization (Riches, 1943*a*, *b*); the small catheter, size 16F, is inserted into the distended bladder through a small incision in the abdominal wall. Its point of entry is opposite the highest point of bladder dullness or the mid-point between the umbilicus and the symphysis, whichever is the lower. Its direction is obliquely downwards and backwards. It is rapid, requires no great technical skill but only a modicum of common sense, and is quite safe provided that the bladder is distended. If this is not the case the bladder must be exposed through a short incision before the catheter is introduced. The catheter must be changed after fourteen days and subsequently once a week. Any straight rubber catheter of the same size can be used and no introducer is required, the only necessity being asepsis. If the catheter is to be retained for many weeks it is replaced by one a little larger, size 20F being usually adopted.

Cases treated by this method have proved satisfactory, and it would appear that the principle of suprapubic drainage is not at fault.

TIDAL DRAINAGE

When drainage has been established it must be continuous; any obstruction of the catheter will make it act as a cork and will be followed by signs of infection. This applies particularly to cases previously infected by urethral catheterization. The best way of ensuring continuity is by efficient tidal drainage. The apparatus we use, the "double Y", is convenient because it incorporates a cystometer. An irrigating fluid designed to keep the urine acid is preferable. Where there is a tendency to phosphatic deposition the solution G of Suby (1942) is of most value.

The value of tidal drainage has been questioned by those who maintain that small doses of sulphonamides are more effective in preventing infection. Unfortunately sulphonamides cannot be continued indefinitely whilst tidal drainage can. To me one of the most encouraging facts about it is that of the few men discharged with permanent suprapubic tubes most continue to keep their tidal drainage going every night.

It is often asked why suprapubic drainage gives less liability to serious infection than urethral drainage. It may be stated at once that suprapubic drainage does not prevent infection of the bladder; whenever a tube is passed into the bladder and retained there infection is bound to gain entrance in time. With a catheter in the urethra, however, there is always urethritis and it has been shown that the path of ascending infection is by direct lymphatic spread from the deep urethra by peri-ureteral lymphatics to the kidneys. There is no such direct lymphatic connexion from the track of a suprapubic catheter to the kidneys, and ascending infection is much less common from a bladder which is draining freely. Infection of the bladder is not lethal but infection of the kidneys is.

The effect of inadequate drainage.—The policy of absolute non-interference with the bladder has been advocated from time to time, the bladder being left alone until the stage of retention with overflow is followed by automatic micturition. This certainly obviates the risk of instrumental infection but it does carry the dangers of prolonged overdistension. The time before periodic reflex micturition is established is uncertain and may be more than a year in cauda equina lesions and serious renal damage may ensue if the bladder is not drained. Perhaps the worst danger lies in irregular intermittent catheterization which leads to infection without securing continuous drainage.

A woman of 25 developed a cauda equina lesion following a spinal anæsthetic. She was catheterized occasionally but allowed to go home with urinary incontinence, before periodic reflex micturition was established. I saw her six months later when she had a distended bladder with overflow incontinence and gross urinary infection. The right kidney was hardly secreting, the left was dilated, and the bladder held 17 oz. (fig. 1). Suprapubic catheterization was performed and she was put on tidal drainage. After three weeks the right kidney was secreting, the left being still dilated. At this time a cystogram (fig. 2) showed a conical bladder with a reflux up a dilated and tortuous right ureter into a dilated renal pelvis. After nine months she was able to pass all fluid from her bladder except 1¼ oz.: the suprapubic catheter was removed, the fistula never leaked and was closed in a day. After closure the intravenous pyelogram showed good function on both sides with only a little dilatation on the right (fig. 3). When seen after a year the pyelogram was unchanged, the urine was clear, and she was able to empty her bladder and was not incontinent. The duration of suprapubic drainage in this case was nine months, and no fixed time limit can be laid down. *(See illustrations next page.)*

It is our aim at present to close the bladder in all cauda equina lesions when it can be done with safety, and we are closing more of those with cord lesions than formerly. In these the patient must wear a urinal, but the psychological effect of a closed bladder is very great. The safety factors are a satisfactory general condition, a small residual urine (probably not more than 2 oz.) and relatively little infection. When the fistula has been closed any slight vesical infection will often clear up provided there is not much residual urine.

In a conus lesion in a girl of 20 with permanent paralysis a small suprapubic catheter was retained for two years. On its removal the fistula was dry in two days and she regained a continent bladder, emptying by straining with less than 2 oz. of residual urine and no infection. She can sleep through the night without passing urine and goes for four hours by day.

Closure of the small high fistula after suprapubic catheterization is rapid and spontaneous; closure of a fistula after a low cystotomy is prolonged and it usually needs excision. Most of the cases admitted to the Centre have already got a suprapubic cystotomy done by the older methods and the fistula is often adherent to the symphysis. These tax the surgeon's resources considerably when the time comes for their closure. Thus there has been little opportunity for the use of serum needle inserted well above the pubes. This may if necessary be repeated once, but frequent aspiration is likely to lead to extravasation. Under peacetime conditions however it should rarely be impossible to get the patient into hospital within twenty-four hours; during the war mobile teams often made surgical treatment available in a shorter time.

Let us then assume that twenty-four hours have elapsed, the bladder is distended, there has been no voluntary or automatic micturition and the surroundings are such that reasonable asepsis is possible. Is the bladder to be drained by urethral or suprapubic catheter? I may say at once that I strongly advocate the suprapubic route for general use. It is true that we have had one or two cases received into the Spinal Injuries Centre at Stoke Mandeville very soon after their injury where the urethral catheter combined with tidal drainage and adjuvant measures have been used successfully, but they form a very small minority. They require infinite care and unlimited time, and their supervision is a one-man job. Incidentally paraplegics should never be catheterized by an orderly. When drainage is established it must be adequate and regular or continuous; it must be such as to prevent extreme contraction or excessive dilatation of the bladder, there must be no urinary leakage, and above all it must avoid the possibility of serious infection. The method must be one which the nursing staff can understand and care for. The method I advocate is the introduction of a small suprapubic catheter into the upper part of the distended bladder. Its track must be oblique, and the catheter must fit closely. I do not refer to suprapubic cystotomy as usually performed. We all have often been horrified by the large tube placed at the bottom of a long incision with urine leaking around it and infection getting in. At a later stage the track becomes adherent to the pubes and closure is at best delayed and at worst impossible. Moreover the bladder is allowed to contract down to a small capacity. and any periodic reflex micturition which may ultimately develop is useless because of its frequency. Examples have been shown previously (Riches, 1944).

I have described elsewhere the method of suprapubic catheterization (Riches, 1943*a*, *b*); the small catheter, size 16F, is inserted into the distended bladder through a small incision in the abdominal wall. Its point of entry is opposite the highest point of bladder dullness or the mid-point between the umbilicus and the symphysis, whichever is the lower. Its direction is obliquely downwards and backwards. It is rapid, requires no great technical skill but only a modicum of common sense, and is quite safe provided that the bladder is distended. If this is not the case the bladder must be exposed through a short incision before the catheter is introduced. The catheter must be changed after fourteen days and subsequently once a week. Any straight rubber catheter of the same size can be used and no introducer is required, the only necessity being asepsis. If the catheter is to be retained for many weeks it is replaced by one a little larger, size 20F being usually adopted.

Cases treated by this method have proved satisfactory, and it would appear that the principle of suprapubic drainage is not at fault.

TIDAL DRAINAGE

When drainage has been established it must be continuous; any obstruction of the catheter will make it act as a cork and will be followed by signs of infection. This applies particularly to cases previously infected by urethral catheterization. The best way of ensuring continuity is by efficient tidal drainage. The apparatus we use, the "double Y", is convenient because it incorporates a cystometer. An irrigating fluid designed to keep the urine acid is preferable. Where there is a tendency to phosphatic deposition the solution G of Suby (1942) is of most value.

The value of tidal drainage has been questioned by those who maintain that small doses of sulphonamides are more effective in preventing infection. Unfortunately sulphonamides cannot be continued indefinitely whilst tidal drainage can. To me one of the most encouraging facts about it is that of the few men discharged with permanent suprapubic tubes most continue to keep their tidal drainage going every night.

It is often asked why suprapubic drainage gives less liability to serious infection than urethral drainage. It may be stated at once that suprapubic drainage does not prevent infection of the bladder; whenever a tube is passed into the bladder and retained there infection is bound to gain entrance in time. With a catheter in the urethra, however, there is always urethritis and it has been shown that the path of ascending infection is by direct lymphatic spread from the deep urethra by peri-ureteral lymphatics to the kidneys. There is no such direct lymphatic connexion from the track of a suprapubic catheter to the kidneys, and ascending infection is much less common from a bladder which is draining freely. Infection of the bladder is not lethal but infection of the kidneys is.

The effect of inadequate drainage.—The policy of absolute non-interference with the bladder has been advocated from time to time, the bladder being left alone until the stage of retention with overflow is followed by automatic micturition. This certainly obviates the risk of instrumental infection but it does carry the dangers of prolonged overdistension. The time before periodic reflex micturition is established is uncertain and may be more than a year in cauda equina lesions and serious renal damage may ensue if the bladder is not drained. Perhaps the worst danger lies in irregular intermittent catheterization which leads to infection without securing continuous drainage.

A woman of 25 developed a cauda equina lesion following a spinal anæsthetic. She was catheterized occasionally but allowed to go home with urinary incontinence, before periodic reflex micturition was established. I saw her six months later when she had a distended bladder with overflow incontinence and gross urinary infection. The right kidney was hardly secreting, the left was dilated, and the bladder held 17 oz. (fig. 1). Suprapubic catheterization was performed and she was put on tidal drainage. After three weeks the right kidney was secreting, the left being still dilated. At this time a cystogram (fig. 2) showed a conical bladder with a reflux up a dilated and tortuous right ureter into a dilated renal pelvis. After nine months she was able to pass all fluid from her bladder except 1¼ oz.; the suprapubic catheter was removed, the fistula never leaked and was closed in a day. After closure the intravenous pyelogram showed good function on both sides with only a little dilatation on the right (fig. 3). When seen after a year the pyelogram was unchanged, the urine was clear, and she was able to empty her bladder and was not incontinent. The duration of suprapubic drainage in this case was nine months, and no fixed time limit can be laid down. *(See illustrations next page.)*

It is our aim at present to close the bladder in all cauda equina lesions when it can be done with safety, and we are closing more of those with cord lesions than formerly. In these the patient must wear a urinal, but the psychological effect of a closed bladder is very great. The safety factors are a satisfactory general condition, a small residual urine (probably not more than 2 oz.) and relatively little infection. When the fistula has been closed any slight vesical infection will often clear up provided there is not much residual urine.

In a conus lesion in a girl of 20 with permanent paralysis a small suprapubic catheter was retained for two years. On its removal the fistula was dry in two days and she regained a continent bladder, emptying by straining with less than 2 oz. of residual urine and no infection. She can sleep through the night without passing urine and goes for four hours by day.

Closure of the small high fistula after suprapubic catheterization is rapid and spontaneous; closure of a fistula after a low cystotomy is prolonged and it usually needs excision. Most of the cases admitted to the Centre have already got a suprapubic cystotomy done by the older methods and the fistula is often adherent to the symphysis. These tax the surgeon's resources considerably when the time comes for their closure. Thus there has been little opportunity for the use of suprapubic catheterization in the war cases, but I have used it in other paraplegics and have found it trustworthy.

Even with formal suprapubic cystotomy which has been extensively used during the latter part of the war the results have been incomparably better than they were when urethral catheterization was the rule, and the results we are getting now are a great advance on those I saw in the Spinal Injuries Centres in 1942. I am sure they can be improved still further by the adoption of the small high suprapubic catheter in place of the large low cystotomy tube for both the initial and subsequent treatment of the bladder until automatic action is established.

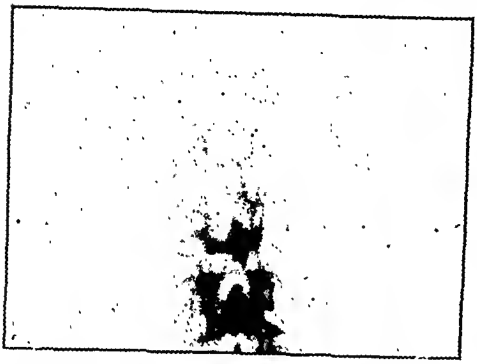


FIG. 1.—Cauda equina lesion without drainage. Excretion urogram (45 min. film). No secretion on right, hydronephrosis on left.

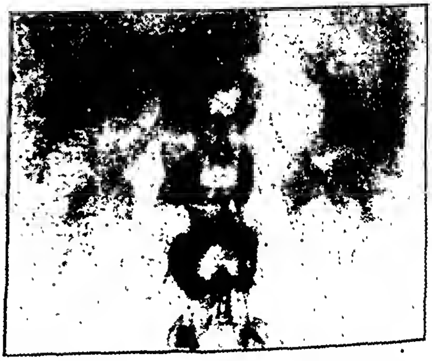


FIG. 3.—Same case nine months after suprapubic catheterization (15 min. film). The bladder is now closed.

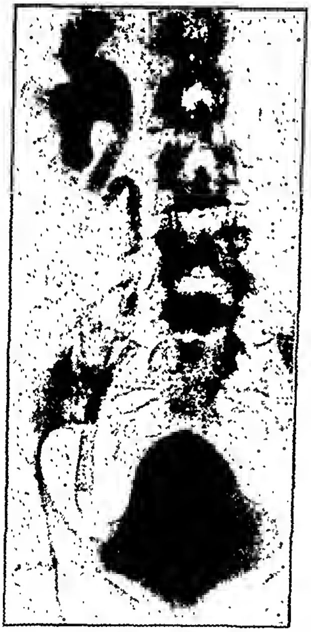


FIG. 2.—Same case; cystogram showing right ureteric reflux.

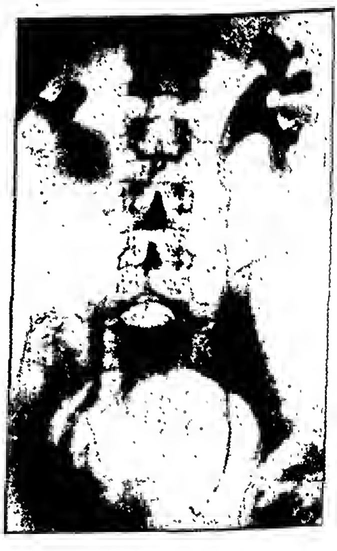


FIG. 4.—Cauda equina lesion treated by urethral catheterization. Pyelogram showing bilateral hydronephrosis and hydro-ureter.

I have already mentioned that one or two cases treated by urethral catheterization at the Centre from the outset have obtained excellent results, but I still feel it is not a method for general use. A cauda equina lesion (fig. 4) was treated elsewhere by urethral catheter; he is clinically well and has a good automatic bladder, but his urine is infected and pyelography shows both kidneys to be dilated, a poor augury for his future.

Stone formation.—Infection, recumbency and dilatation of the upper urinary tract are potent factors in producing renal calculi, and the stones formed in these cases are generally hard, and extensive. Although they are phosphatic they show little tendency to disappear when the patient is able to be up and about, and they must be removed surgically. Stones in the bladder can sometimes be dissolved by the use of solution G in the suprapubic tidal drain.

After removing renal stones it is an advantage to leave in a nephrostomy tube for several weeks so that daily lavage with solution G can be carried out, but I have had no success in dissolving formed renal calculi by this method.

REFERENCES

RICHES, E. W. (1943*a*) *Lancet* (ii), 128.
—— (1943*b*) *Brit. J. Surg.*, 31, 135.
—— (1944) *Proc. R. Soc. Med.*, 37, 77.
SUBY, H. I., SUBY, R. M., and ALBRIGHT, F. (1942) *J. Urol.*, 48, 549.

Dr. D. Whitteridge: *Physiological disturbances produced by distension of the bladder.*—Clinically, the most conspicuous feature of the disturbances produced by distension of the bladder in patients with high spinal lesions was the flushing of the face and neck. A conventional multiple-junction skin thermometer was made up, and used for the recording of the temperature in the feet, rectum, trunk and neck. The rectal temperature was found to rise slightly, that of the neck rose two to three degrees, while that of the feet fell sharply. A redistribution of blood on a considerable scale therefore seemed to be taking place, and arrangements were made to record at short intervals blood-pressure and pulse-rate in addition to the skin temperature. The usual difficulties in the interpretation of skin temperature changes led us to follow the peripheral blood flow plethysmographically, and a transportable apparatus was constructed for the photographic recording of pulse volumes and finger blood flow (by the method of Wilkins, Doupe and Newman, 1937), bladder pressure, ear volume and blood-pressure. The method of Evans and Mendelssohn (1946) was adapted by Mr. R. W. Gilliatt for photographic recording.

When the bladder was filled slowly, there was a profound finger and toe constriction, accompanied by a rise in blood-pressure, as soon as active contractions of the detrusor muscle began. In patients with lesions above T. 5, the rise in systolic pressure was 70 to 160 mm.Hg, and the diastolic rise was 50 to 90 mm.Hg. There was a sharp initial fall in the pulse-rate, which later rose towards normal while the bladder distension continued. The volume of the pulse in the ear rose, as did its temperature, even in a patient with a complete lesion at C. 8.

In patients with lesions at or below T. 6, the picture was rather different. There was the same fall in temperature of the legs, and profound fall in the pulse volume in the toes, with even greater falls in the pulse-rate, but the blood-pressure did not rise more than 30 mm.Hg, and the blood flow in the fingers increased.

When the bladder was suddenly distended with 60 c.c. of water at body temperature, vasoconstriction began in five to six seconds, and was followed almost immediately by a rise in blood-pressure.

It would seem that the essential difference between the two groups of patients is that in those with the lower lesions vasomotor regulation is still possible, since there are still large areas of the vascular bed which can be used by the vasomotor centre for compensatory vasodilatation. With lesions above T. 5, the area controlled by the vasomotor centre is greatly reduced, and with lesions above T. 1, the only efferent path from the vasomotor centre is formed by the cardio-inhibitory fibres of the vagus. To make matters worse, the cardio-accelerator fibres which arise from the isolated cord are probably being excited.

Distension of the rectum by a balloon caused a similar rise in blood-pressure, with vasoconstriction, sweating and pilomotor activity in the arms. These effects were rather transient, while those elicited by distension of the bladder persisted as long as distension was maintained. Distension of parts of the alimentary tract has already been shown to produce vasoconstriction in the toe, and, to a lesser extent, in the finger (Carmichael, Doupe, Harper and McSwiney, 1939). From their evidence, it is likely that the vasoconstriction which they observed is due to a reflex rather than to a central phenomenon related to pain. There can be no question that our phenomenon is due to a spinal reflex, and it seems likely that distension of some hollow viscera can give rise to a peripheral vasoconstriction, which, in these patients, can spread to involve the whole of the sympathetic vasomotor outflow of the isolated cord.

REFERENCES

CARMICHAEL, E. A., DOUPE, J., HARPER, A. A., and MCSWINEY, B. A. (1939) *J. Physiol.*, 95, 276.
EVANS, D. S., and MENDELSSOHN, K. (1946) *Brit. med. Bull.*, 4, 99.
WILKINS, R. W., DOUPE, J., and NEWMAN, H. W. (1937) *Clin. Sci.*, 3, 403.

Dr. P. H. A. Jonason: The rehabilitation of high lesions is found difficult owing to vasomotor disturbances.

That cerebral anæmia due to postural changes causes fainting attacks in convalescent patients following any illness which entails a long rest in bed is well known.

However, very little has been published about details of the effects of changes of posture on the vasomotor system of spinal man.

Experimental work on animals on this subject was initiated in this country by Leonard Hill and Barnard in 1897. It seemed worth while studying this problem on a number of paraplegics at various levels, the more so as some of the patients showed more difficulty in adapting themselves to the upright position than others. It was found that whilst spinal cases with more distal cord lesions did not differ from other non-spinal convalescent cases in their vasomotor reactions those with high thoracic and cervical cord lesions showed more profound and longer lasting effects to postural changes. In this short report details are given only of our findings on the pulse-rate, diastolic and systolic blood-pressures and subjective sensations noticed by the patient.

Method.—In order to produce maximal effects a tilting table was used. The apparatus consisted of a standard army stretcher fitted to a frame enabling the stretcher with the patient on it to be rapidly tilted from the horizontal position to the vertical feet-down position. The patient lies on a sorbo rubber mattress and is comfortably secured. Great care was taken to avoid any undue pressure which might obstruct even superficial blood circulation and respiratory movement; the head, neck, arms and upper trunk being completely free. All cases with indwelling suprapubic catheters were fitted with bottles to allow an unobstructed bladder drainage and so avoid the converse effects of a distended viscus below the level of the lesion.

Repeated recordings of the pulse-rate and the blood-pressure were then taken until three consecutive recordings at one-minute intervals showed a constant pulse-rate and blood-pressure.

These recordings were taken by independent observers, both taking part in observing changes in the patients themselves. The patients co-operated extremely well in stating effects that they themselves noticed such as dimness of vision, tinnitus and feelings of faintness.

Once the blood-pressure and pulse-rate were stabilized the table was tilted from the horizontal position to the vertical feet-down position. This alteration of position took only one and a half seconds and immediate recordings were taken at one-minute intervals until either the patient complained of unpleasant feelings, or showed signs of syncope or twenty minutes had elapsed. At the end of this time, the table was again returned to the horizontal position and recordings repeated until the blood-pressure and pulse-rate had returned to normal or all side-effects had passed off.

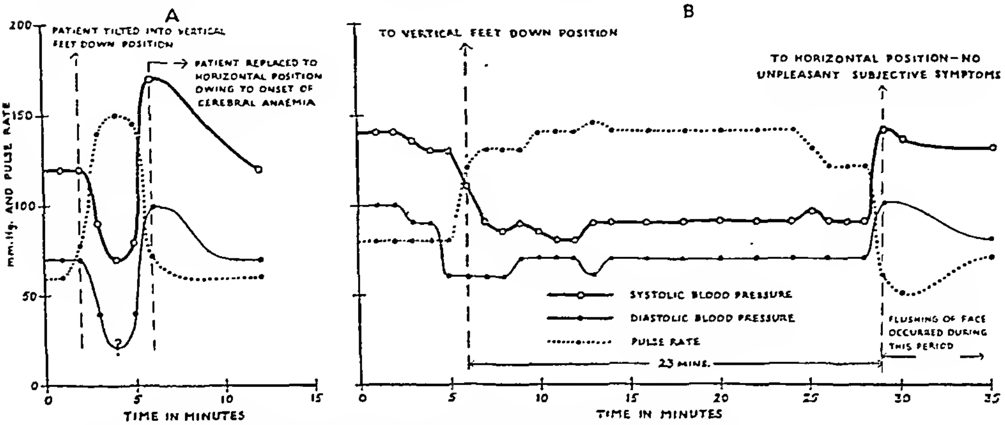


CHART I.—Patient H. H., aged 24. Transverse spinal syndrome at T. 4.

Experiment A was carried out on 30.5.46 and lasted only four minutes in the vertical feet-down position before cerebral anæmia set in.

Experiment B was carried out on 18.9.46 and no ill effects occurred even after maintaining the vertical feet-down position for twenty-three minutes.

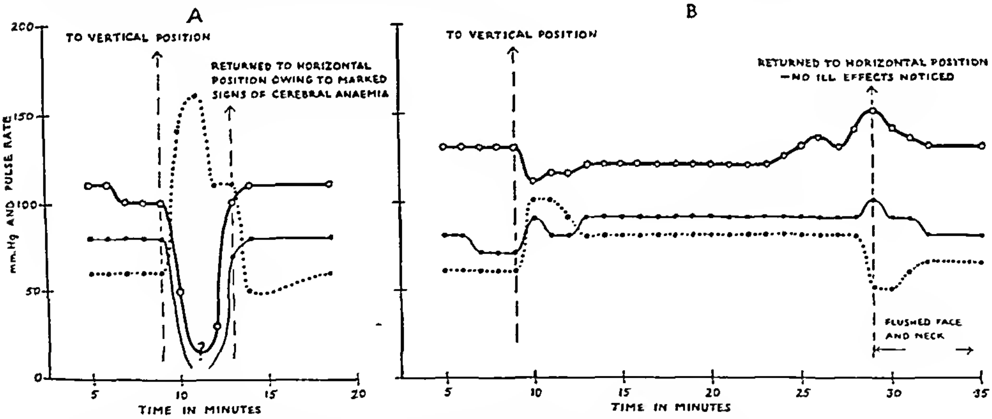


CHART II.—Patient A. H., aged 23. Complete transverse spinal syndrome at T. 3.

Experiment A was started on 30.8.46 and lasted only four minutes, owing to profound cerebral anæmia causing unpleasant subjective symptoms.

Experiment B on 29.10.46. There were no ill effects after twenty minutes, the systolic blood-pressure actually increasing.

Dr. W. Ritchie Russell: In the care and rehabilitation of traumatic paraplegia neither the neurologist nor the orthopædic surgeon is able to deal properly with these cases with the facilities usually at their disposal, and it is clear that the argument for their segregation in special Centres is indisputable. It is only in the special Centre that the sometimes conflicting interests of the care of the fractured centre for compensatory vasodilatation. With lesions above T. 5, the area controlled by the vasomotor centre is greatly reduced, and with lesions above T. 1, the only efferent path from the vasomotor centre is formed by the cardio-inhibitory fibres of the vagus. To make matters worse, the cardio-accelerator fibres which arise from the isolated cord are probably being excited.

Distension of the rectum by a balloon caused a similar rise in blood-pressure, with vasoconstriction, sweating and pilomotor activity in the arms. These effects were rather transient, while those elicited by distension of the bladder persisted as long as distension was maintained. Distension of parts of the alimentary tract has already been shown to produce vasoconstriction in the toe, and, to a lesser extent, in the finger (Carmichael, Doupe, Harper and McSwiney, 1939). From their evidence, it is likely that the vasoconstriction which they observed is due to a reflex rather than to a central phenomenon related to pain. There can be no question that our phenomenon is due to a spinal reflex, and it seems likely that distension of some hollow viscera can give rise to a peripheral vasoconstriction, which, in these patients, can spread to involve the whole of the sympathetic vasomotor outflow of the isolated cord.

REFERENCES

CARMICHAEL, E. A., DOUPE, J., HARPER, A. A., and MCSWINEY, B. A. (1939) *J. Physiol.*, 95, 276.
EVANS, D. S., and MENDELSSOHN, K. (1946) *Brit. med. Bull.*, 4, 99.
WILKINS, R. W., DOUPE, J., and NEWMAN, H. W. (1937) *Clin. Sci.*, 3, 403.

Dr. P. H. A. Jonason: The rehabilitation of high lesions is found difficult owing to vasomotor disturbances.

That cerebral anæmia due to postural changes causes fainting attacks in convalescent patients following any illness which entails a long rest in bed is well known.

However, very little has been published about details of the effects of changes of posture on the vasomotor system of spinal man.

Experimental work on animals on this subject was initiated in this country by Leonard Hill and Barnard in 1897. It seemed worth while studying this problem on a number of paraplegics at various levels, the more so as some of the patients showed more difficulty in adapting themselves to the upright position than others. It was found that whilst spinal cases with more distal cord lesions did not differ from other non-spinal convalescent cases in their vasomotor reactions those with high thoracic and cervical cord lesions showed more profound and longer lasting effects to postural changes. In this short report details are given only of our findings on the pulse-rate, diastolic and systolic blood-pressures and subjective sensations noticed by the patient.

Method.—In order to produce maximal effects a tilting table was used. The apparatus consisted of a standard army stretcher fitted to a frame enabling the stretcher with the patient on it to be rapidly tilted from the horizontal position to the vertical feet-down position. The patient lies on a sorbo rubber mattress and is comfortably secured. Great care was taken to avoid any undue pressure which might obstruct even superficial blood circulation and respiratory movement; the head, neck, arms and upper trunk being completely free. All cases with indwelling suprapubic catheters were fitted with bottles to allow an unobstructed bladder drainage and so avoid the converse effects of a distended viscus below the level of the lesion.

Repeated recordings of the pulse-rate and the blood-pressure were then taken until three consecutive recordings at one-minute intervals showed a constant pulse-rate and blood-pressure.

These recordings were taken by independent observers, both taking part in observing changes in the patients themselves. The patients co-operated extremely

Section of Orthopædics

President—V. H. ELLIS, F.R.C.S.

[*November* 5, 1946]

Protrusion of Intervertebral Discs

By R. H. YOUNG, F.R.C.S.

THIS is an Address which B. H. Burns and I prepared before the International Orthopædic Congress held on October 3, 1946, and which he delivered in Brussels.

Burns and I have had the opportunity at a war hospital, of dealing with a considerable number of patients with sciatica and backache.

Those who have been reluctant to accept that operation is a cure for sciatica, have the habit of remarking "what used to happen to these cases before their discs were removed? Nearly all of them got better" they would say.

We have the records of many cases of sciatica which were treated by all the methods then in vogue in the years before we operated. 248 of them were available for follow-up last year.

PATIENTS WITH SCIATICA

		Still in pain or having attacks %	Symptomless %	Total
Not operated on				
First seen 1939-42. Followed up 1945		79	21	248
Operated on				
1941-45 Followed up 1946	Improved 11% No better 9%	20	80	310

Since 1942 all but 9 patients with severe sciatica have been operated on.

The table shows that 4 out of 5 were still having attacks; also, that since we began operating on them in 1941 the position is reversed, 80% are now symptomless and 20% still have some pain.

All but 9 cases of severe sciatica have been operated on.

The conditions found at laminectomy have been as follows:

CONDITIONS FOUND AT LAMINECTOMY FOR SCIATICA AND BACKACHE

Disc lesions	470
Spondylolisthesis	20
Root irritation from osteo-arthritic lip	11
Root irritation from narrowed foramen	6
Cauda equina tumour	1
Abscess from osteomyelitis	1
Unknown	24
TOTAL	533

Since we have operated on nearly every severe case of sciatica it follows that protrusion of a disc is by far the commonest cause of sciatica. A bad second is spondylolisthesis.

Also we consider that a disc lesion is the commonest cause of recurrent backache, but the proof of this is not quite so definite as we have not checked our diagnosis by operation so often. Nevertheless we have operated on 45 patients with backache only and we found, in all but 2 of these, a lesion of a disc. The reason why this number is relatively small is that those patients with backache alone are seldom bad enough to require operation. They tend to get better, or if they get worse they develop sciatica. Further the majority of patients with sciatica due to protrusion of a disc, have, in their early stages, signs and symptoms of backache only.

EARLIEST SYMPTOMS IN 470 PROVED DISC LESIONS

Backache	68%
Sciatica	24%
Backache and sciatica	8%

bones of the spine, the anæsthetic skin, and the patient's morale are likely to be properly balanced.

Dr. P. W. Nathan asked Mr. Riches whether, if an automatic bladder is obtained within a few weeks or even a few months, it would not be preferable to close the suprapubic cystotomy, and continue treatment with tidal drainage, manual expression and intermittent catheterization, combined with sulphadiazine. Such a line of treatment seems possible now that there is such effective therapy in the form of sulphadiazine and the newer sulpha drugs. During the campaign in Italy he found that when sulphadiazine was given to cases with suprapubic cystotomies, the urine could be kept sterile; it remained free from *B. coli*, and microscopically contained less than 10 leucocytes per field.

Dr. Giles Romanes: I have treated one case of bladder stones in a paraplegic patient with solution G on two occasions. It was able to dissolve a phosphatic calculus which was approximately the size of a marble in ten days. Three days later an X-ray proved that the stone was absent. In my experience the saving of time of four weeks in the dissolution of a stone is entirely due to the method of administering the solution G. I used a double suprapubic catheter so that the solution G was poured directly on to the stone. The catheter is made by taking a No. 34 de Pezzer and cutting an oblique nick in the wall about 2½ in. from the peripheral end. The hole made is valvular and a fine prostatic soft rubber catheter is inserted down the lumen of the de Pezzer projecting 2 in. through the proximal end. This allows for the stretching of the whole over the introducer. The external junction between the catheters is sealed off with ordinary puncture-mending rubber solution. This method completely eliminates any dilution of the active agent with urine as is bound to happen when it is administered by means of a tidal apparatus.

Mr. Riches, in reply to Dr. Nathan, stated that the bladder must be drained because it is paralysed. He did not wish to drain it for as long as two years but the period before recovery was uncertain and it was better to maintain drainage until the maximum recovery was obtained as shown by cystometry, power of emptying and lack of residual urine. He agreed that urethral drainage would give earlier recovery than suprapubic drainage if it could be kept free from infection, but experience in its general use showed that it could not.

He agreed that solution G must come into constant and intimate contact with stones if it was to be effective.

The President: We began the second World War with a much better knowledge of traumatic paraplegia as a result of the classical work of Head and Riddoch. However, the ultimate outlook for these patients seemed no brighter than it had been following the first World War until the Peripheral Nerve Injuries Committee, with Dr. George Riddoch as chairman, recommended setting up Spinal Injuries Centres in this country, of which that run by the Ministry of Pensions at Stoke Mandeville Hospital became the best known. Dr. Guttmann has shown us that not only has the expectation of life of these patients been materially improved, but that with appropriate methods of treatment and rehabilitation, a degree of functional recovery may be achieved that a few years ago would not have seemed possible. This discussion has shown that the successful treatment of the paraplegic bladder depends, as a rule, not so much on the method used as on the skill of the personnel who carry out the treatment. Mr. Riches has made a strong case for high suprapubic catheterization as a routine measure in these cases. Whatever method is adopted it is clear that a urologist should co-operate in the treatment of these cases from the beginning.

PATHOLOGY

At operation we have found that there are two kinds of protrusion. One is a protrusion of the nucleus pulposus and the other is a tear of the annulus fibrosus. In a nuclear protrusion the annulus is intact and the nucleus comes out between the top or bottom of the annulus and the vertebral body. Fig. 1 illustrates the nuclear protrusion.

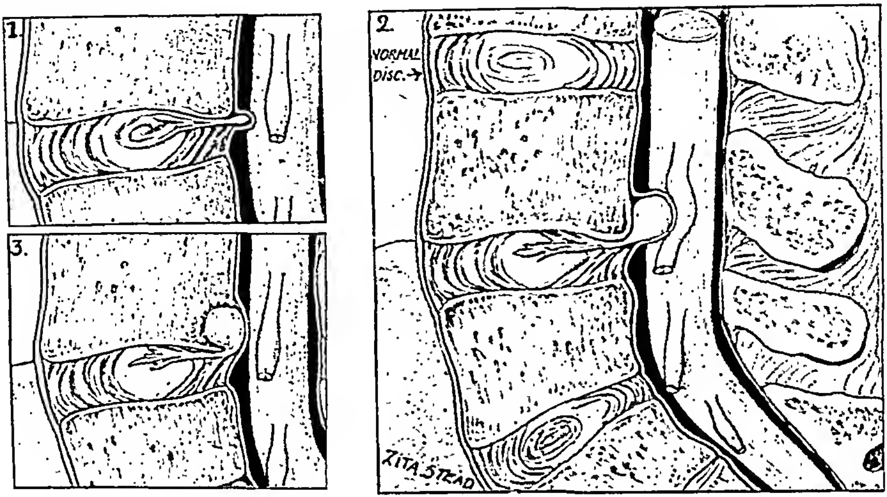


FIG. 1.

1.—Small protrusion. At this stage it can pop in and out. We have pushed them back at operation. When reduced it will be missed. Therefore one should operate only during an attack. 2.—Larger protrusion. This causes pressure on nerve and sciatica. 3.—A later stage of 2. The protrusion has eroded the vertebral body—the pressure on the nerve root is therefore released—the sciatica is relieved, but the patient is left with a lame back. This lesion has sometimes been found in patients with a "lame back" following a prolonged attack of acute sciatica which has gradually cleared up.

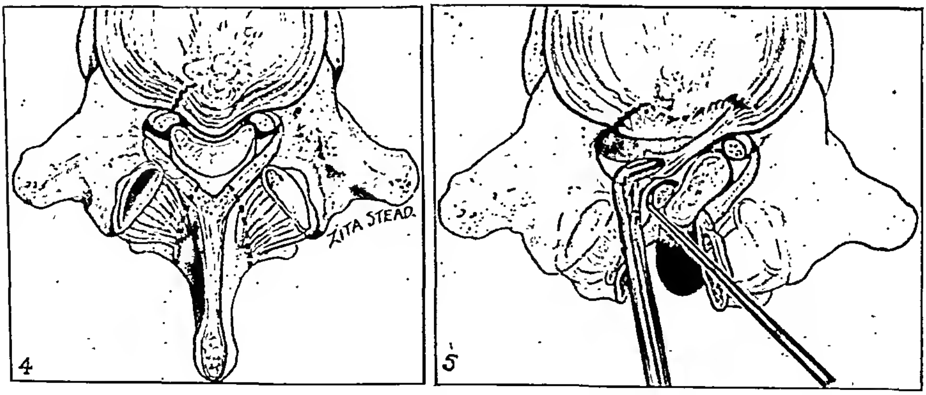


FIG. 2.

Fig. 2 illustrates an annular tear. The whole thickness of the annulus is torn. It mimics a torn meniscus, and swings in and out. It is not only necessary to remove the piece of torn annulus, but all the nucleus must be removed as well, like removing the charge from a shell. Not doing so was the cause of some of our early failures. In our opinion it is not necessary, like Dandy, to remove the whole disc—all of the annulus—in an attempt to get ankylosis.

The pain may be in the back alone for months and even years before the sciatica develops. Our general views on backache and its causes are as follows:

(1) Chronic or recurrent low backache without physical signs = visceral lesions or neurosis.

(2) Chronic or recurrent low backache with physical signs = disc lesion unless X-ray shows other conditions, such as spondylolisthesis or spondylitis.

Diagnosis.—A disc lesion may be suspected from the history. In fact, a diagnosis can often be made over the telephone from a story of recurrent attacks of backache and stiffness. Suspicions are confirmed if there are back signs as well. These are restriction of forward bending whilst sideways bending is free. The diagnosis, so long as the X-ray is negative, can be made on this sign alone.

(1) In sciatic scoliosis lateral bending is free to the side which increases the deformity.

(2) Sciatic scoliosis is always due to a disc lesion.

Neurological signs are only of value as confirmation. 40% of patients operated on by us have had none. Surgeons by insisting on their presence before a positive diagnosis of a disc protrusion is made are apt, by their delay, to prolong the patient's suffering unnecessarily.

We only operate on about half the patients we diagnose as having a disc lesion. In a first attack, the patient is put to bed for three weeks and if the pain persists an operation is recommended. Our threshold for operation is lower than it used to be, and we feel justified in this from the fact that none of our 533 laminectomies have been made worse. The operation is without danger, although it is not without difficulty.

If it is decided to operate it would be a help to know which disc is at fault, but although we know that 95% occur at the lowest two discs, it is impossible to localize the lesion to either of these two. It has often been claimed that localization is possible by neurological signs, but the following table shows that this is not so.

FREQUENCY OF MAIN NEUROLOGICAL SIGNS IN PROVED DISC LESIONS
With neurological signs, 61%; without neurological signs, 39%

	Ankle-jerk		
	Normal	Diminished	Absent
5/1 disc ..	39	24	37
4/5 disc ..	67	20	13
3/4 disc ..	2 cases—normal		

	Sensation	
	Normal	Diminished outer border of foot
5/1 disc ..	58	39
4/5 disc ..	70	27
3/4 disc ..	2 cases—normal	

3% have diminished sensation inner border of foot.

Thus neurological signs are useless for localization. 39% of the patients have no neurological signs, and, of the main neurological signs, changes in the ankle-jerk and changes in sensation can be present in a similar proportion in both 4/5 and 5/1 disc.

Further we have had no help from myelography either with opaque media or with air. We consider that the procedure is misleading and if lipiodol is used, dangerous, as it leads to arachnoiditis.

Therefore, we remove the whole of the fifth lamina and adjacent ligamenta flava, so as to have free access to both of the lower two spaces. We have not found that this led to a weakened back.

We operate with the patient lying on his side. This has many advantages:

(*a*) It is the easiest way to flex the spine (Pridie has him like a rabbit about to take off). (*b*) The blood runs away from the bottom of the wound. (*c*) The patient is much less shocked than when lying on his face with pressure on the solar plexus.

Incidentally, it is much more comfortable as operators can sit and onlookers can see more easily.

attempt to solve it by using a parallel nail and graft, the technique of which was simplified by Wardle's ingenious and simple modification of a trifin nail.

Comparison with Wardle.—The method, although not so simple as that used by Wardle, is far more effective in that it prevents the nail from cutting out anteriorly through the head of the femur as a result of external rotation of the leg.

It has, in fact, been used as a second operation where a Wardle nail and graft had failed and in this instance held very securely, in spite of the fact that the head had a groove ploughed in it, the breadth of the original nail and graft.

Method.—The trifin nail is introduced by any method with which the surgeon is familiar, but care should be taken that the nail is as vertical as possible and in the centre of the head in the A.P. view and well posterior in the lateral view (fig. 1).

A graft is cut from the opposite tibia, four inches long and half an inch broad, whilst the first X-rays are being developed. Then after a satisfactory position has been obtained for the nail, an opening is made for the graft to be inserted, half an inch above the nail and in front of it, on the lateral femoral cortex just below the greater trochanter. Through this opening which is made with a gouge, a half-inch osteotome is driven in so as to make a path for the graft, which must converge on the line of the nail and pass anterior to it (fig. 2).

This may seem somewhat complicated, but actually with the line of the nail as a guide, it is not as difficult as it sounds. The osteotome is driven in for an estimated distance, depending on the measurements obtained from the X-ray, but in practice fairly consistently 9 cm., and then an X-ray is taken. If this proves satisfactory, in both A.P. and lateral views (figs. 3 and 4) the osteotome is withdrawn and the graft substituted for it.

If it is not satisfactory, necessary adjustments in the alignment of the osteotome are made until a satisfactory position is obtained.

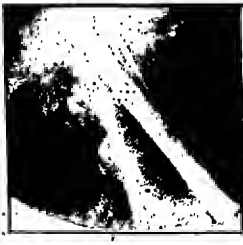


FIG. 1.

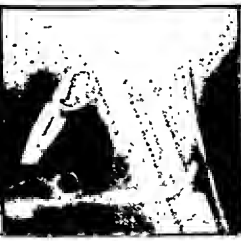


FIG. 2.

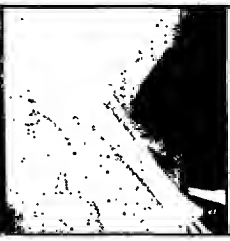


FIG. 3.

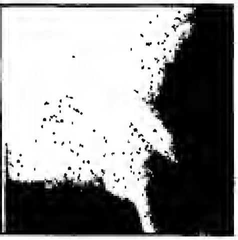


FIG. 4.

FIG. 1.—Ideal position in the A.P. view. The nail will be driven farther in before the operation is completed.

FIG. 2.—Lateral view showing the trifin nail posterior and the osteotome cutting the path for the graft anterior, in the neck of the femur.

FIG. 3.—A.P. view showing graft crossing the line of the trifin nail.

FIG. 4.—Final position, nail driven well in and graft ending in the lower quadrant of the femoral head.

Advantages.—The chief advantage which is obtained by this crossing is that it prevents the nail from breaking out anteriorly, as it has not only to cut a pathway for itself through the head but also has to force the graft to travel in front of it, through a separate portion of the head. In fact the resistance of the graft is sufficient to cause it to fracture before it can be forced to give way.

This must be contrasted with the state which exists when the graft and nail are

In the first table we stated that 9% of our cases were no better and 11% were still having some trouble. We have sought to explain these failures and have concluded that they fall under five causes.

POSSIBLE CAUSES OF FAILURE IN PROVED DISC LESIONS AND TREATMENT RECOMMENDED

Cause	Treatment	Comment
(1) Protrusion of another disc	Re-exploration with removal of protrusion	(1) In 8% of our cases there were two protruded discs. Failure to recognize the second protrusion is a cause of failure
(2) Incomplete removal of nucleus pulposus		(2) Already discussed (*see* p. 11)
(3) Adherent nerve root becoming persistently re-attached	Re-exploration and graft	(3) In old-standing cases with dense adhesions the nerve root may become stuck again
(4) Mechanical arthritis of intervertebral joint ..		(4) Sometimes accompanies a diminished intervertebral space
(5) Diminished joint-space with narrowing of foramen and root compression ..	Facetectomy	(5) Putti's lesion. We do not often find it.

Thus, from our experience, practically all cases of sciatica and most cases of backache can be cured by operation. There is no alternative except rest and that is shown to be much less effective than operation.

Summary.—(1) Almost all sciatica and recurrent backache is due to disc lesions.

(2) The diagnosis can be made on back signs alone.

(3) Only operation offers the patient a definite prospect of cure.

The Crossed Trifin Nail and Graft in the Treatment of Fractures of the Neck of the Femur

By G. K. McKEE, F.R.C.S.

THE simple insertion of a trifin nail in fractures of the neck of the femur, although considered the best initial method of fixation for these fractures, leaves much to be desired as far as end-results are concerned. There are *two main complications* which are responsible for this:

One is *aseptic necrosis* which is a not infrequent cause of failure some months later.

The other is the cutting out of the nail which is an earlier complication than aseptic necrosis and usually occurs a few days or weeks after the operation in spite of the nail being well placed. Even with firm impaction of the fragments and careful after-treatment the nail may not hold and displacement with consequent non-union occurs. Non-union when occurring in old people is a real problem. The two complications of aseptic necrosis and cutting out of the nail are sometimes associated, the nail cutting out because of the degeneration of the head of the femur.

The cutting out of the nail.—This paper is concerned with the cutting out of the nail anteriorly and the introduction of a method of nailing and grafting these fractures which is designed to prevent it.

The problem is not a new one and various contributions have been made in an present series. An example of a successful osteotomy is shown in figs. 1 and 2 (Patient E. H.). In this case the late result is shown after ten years and the lower fragment has grown away from the pelvis. Reossification across the diseased joint after displacement osteotomy may occur for three reasons: First, shearing strains are prevented by osteotomy; secondly, ossification is favoured in ischæmic tissue, and ischæmia may be promoted in the femoral head and neck by division of vessels running in the upper end of the femoral shaft; thirdly, as I have attempted to show in a previous paper (*Proc. R. Soc. Med.*, 1946, **39**, 712), the theory of Lavalle and McCrae Aitken may apply and incision of tuberculous bone may of itself be of benefit. I have frequently performed these osteotomies through tuberculous bone or through a tuberculous abscess. So far from harm having been done, considerable improvement has resulted.

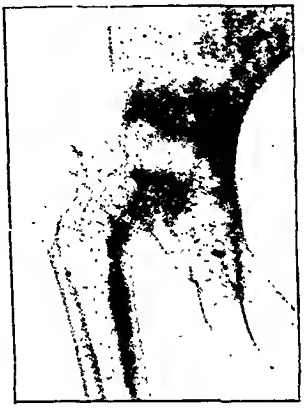


FIG. 1.

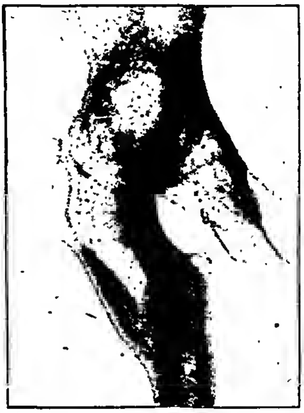


FIG. 2.

E. H., female. FIG. 1.—Tuberculous hip with unsound ankylosis treated by displacement osteotomy. FIG. 2.—Same hip on late follow-up.

Table I shows the result of displacement osteotomy in 21 patients whose hip disease had become quiescent, but in the majority of whom there had developed some deformity or reactivation of disease. Three of these cases were complicated by the presence of chronic discharging sinuses which had not responded to conservative treatment. There was no delay in bone union following osteotomy, and the hips subsequently became stable with healing of the sinuses.

TABLE I.—DISPLACEMENT OSTEOTOMIES WITHOUT GRAFT IN 21 PATIENTS: OPERATIONS TWO OR MORE YEARS AGO: APPARATUS DISCARDED

Firm ankylosis: stable hip	21 cases
Bone ankylosis (13 cases)	Fibrous ankylosis (8 cases)
Children 9, Adults 4	Children 4, Adults 4

In a second series of patients a bone graft was used to augment the displacement osteotomy. An example of this type of osteotomy and graft is shown in figs. 3, 4, 5 (Patient A. H.). I first used the graft as an additional source of osteogenetic tissue, having in mind Lavalle's observation that the results of his operation were better if sliver grafts were inserted into tuberculous bone. The operative method is as follows: An incision is made along the outer and upper aspect of the femoral shaft, and at the tip of the great trochanter it is tailed obliquely backwards in the line of the fibres of the gluteus maximus. In the lower part of the wound the incision is then carried down to the femoral shaft. In the upper part of the wound the gluteal fibres are splinted and retracted. A graft is then cut from the upper end of the parallel with the graft lying anteriorly, for then the nail and graft can travel through the same pathway in the head.

Disadvantages.—The operation time is lengthened when compared with the simple insertion of a nail and a more extensive exposure of the lateral femoral cortex is required.

The post-operative shock is therefore liable to be greater than in the simple insertion of the nail.

For very old and feeble patients this method is best avoided, but if the patient has been up and about prior to the accident and has no added nervous cardiac or pulmonary complications, then it is to be preferred.

The actual cutting of the graft need not add to the length of the operation, as it can be arranged to be done while awaiting the X-rays. Good and quick X-ray technique in the theatre is essential.

Results.—In the course of the last three years I have treated 17 cases by this method and there has been only one failure and this was in a case of a pathological fracture, an osteoclastoma, where there was a rapid bone erosion after the operation. It should not strictly be included in the series.

Intertrochanteric Osteotomy for the Treatment of Tuberculosis of the Hip

By M. C. WILKINSON, M.B.

CONSIDERATION is given in this paper to any oblique osteotomy which achieves the inward displacement of the upper end of the lower fragment of the femur against the under surface of the acetabulum. Such an osteotomy is often intertrochanteric but may be subtrochanteric if there has been much destruction of the acetabular roof by the disease. The chief difficulty of the operation is to produce adequate inward displacement of the lower fragment. This is essential for success. When the bifurcation osteotomy was popular, inward displacement of the lower fragment was effected by placing the limb in marked abduction. In most cases I have avoided this because a fixed abduction deformity may be a crippling condition. Mr. S. L. Higgs has said that an oblique osteotomy should be either above or below the small trochanter, because osteotomy into the psoas tendon makes displacement of the lower fragment very difficult. The osteotomy should be done under X-ray control. By means of a successful osteotomy of this type, stabilization of the hip may frequently be achieved.

Constitutional treatment is essential for tuberculous disease of the hip. Yet an unstable hip is often the result of conservative treatment only, and a proportion of the patients develop reactivation of the disease or deformity. In a series of 50 cases of tuberculosis of the hip treated conservatively which I followed up in 1938, 22 had an unstable hip at the end of treatment. Of these 22 cases, 6 had later to be readmitted for the treatment of fresh disease and 7 for the treatment of deformity. A displacement osteotomy performed when the disease was becoming quiescent might have produced stability of the hip in some of these children. Sir Henry Gauvain used to say that stability followed the bifurcation operation, but insisted that the patient should wear a well-moulded celluloid splint for a sufficient time afterwards. The word stability is used in its clinical sense and means that deformity does not occur and the disease does not reappear after apparatus has been discarded. Bone ankylosis is not necessarily present, but occurred in the majority of cases in the present series. An example of a successful osteotomy is shown in figs. 1 and 2 (Patient E. H.). In this case the late result is shown after ten years and the lower fragment has grown away from the pelvis. Reossification across the diseased joint after displacement osteotomy may occur for three reasons: First, shearing strains are prevented by osteotomy; secondly, ossification is favoured in ischæmic tissue, and ischæmia may be promoted in the femoral head and neck by division of vessels running in the upper end of the femoral shaft; thirdly, as I have attempted to show in a previous paper (*Proc. R. Soc. Med.*, 1946, **39**, 712), the theory of Lavalle and McCrae Aitken may apply and incision of tuberculous bone may of itself be of benefit. I have frequently performed these osteotomies through tuberculous bone or through a tuberculous abscess. So far from harm having been done, considerable improvement has resulted.

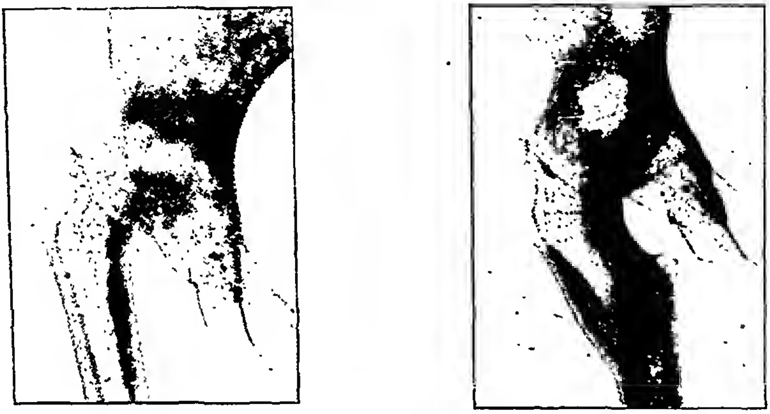


FIG. 1. FIG. 2.

E. H., female. FIG. 1.—Tuberculous hip with unsound ankylosis treated by displacement osteotomy. FIG. 2.—Same hip on late follow-up.

Table I shows the result of displacement osteotomy in 21 patients whose hip disease had become quiescent, but in the majority of whom there had developed some deformity or reactivation of disease. Three of these cases were complicated by the presence of chronic discharging sinuses which had not responded to conservative treatment. There was no delay in bone union following osteotomy, and the hips subsequently became stable with healing of the sinuses.

TABLE I.—DISPLACEMENT OSTEOTOMIES WITHOUT GRAFT IN 21 PATIENTS: OPERATIONS TWO OR MORE YEARS AGO: APPARATUS DISCARDED

Firm ankylosis: stable hip .. .. 21 cases

Bone ankylosis (13 cases)	Fibrous ankylosis (8 cases)
Children 9, Adults 4	Children 4, Adults 4

In a second series of patients a bone graft was used to augment the displacement osteotomy. An example of this type of osteotomy and graft is shown in figs. 3, 4, 5 (Patient A. H.). I first used the graft as an additional source of osteogenetic tissue, having in mind Lavalle's observation that the results of his operation were better if sliver grafts were inserted into tuberculous bone. The operative method is as follows: An incision is made along the outer and upper aspect of the femoral shaft, and at the tip of the great trochanter it is tailed obliquely backwards in the line of the fibres of the gluteus maximus. In the lower part of the wound the incision is then carried down to the femoral shaft. In the upper part of the wound the gluteal fibres are splinted and retracted. A graft is then cut from the upper end of the femur and great trochanter. The oblique osteotomy is then performed with inward displacement of the upper end of the lower fragment. The osteotome is then passed through that part of the great trochanter which has muscles attached to it so that it and the attached muscles can be lifted up and the upper surface of the femoral neck seen or felt. A gouge is passed along the upper surface of the femoral neck

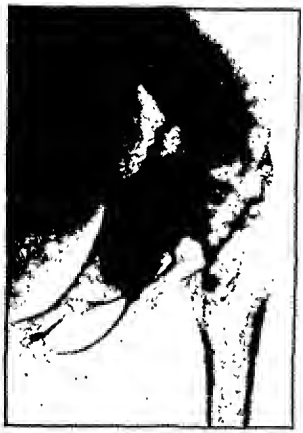


FIG. 3.

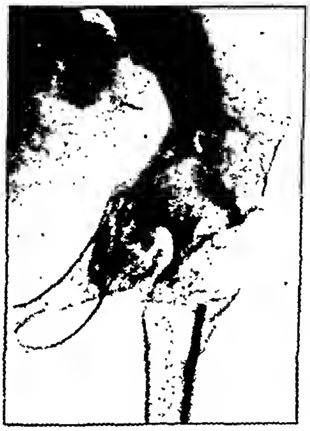


FIG. 4.

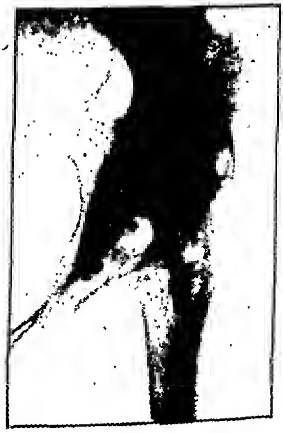


FIG. 5.

A. H., child. FIG. 3.—Pseudarthrosis following tuberculous hip with much destruction of acetabulum.
FIG. 4.—After displacement osteotomy and graft along upper surface of neck. Graft is being absorbed and is difficult to see, but considerable reossification in the destroyed area has occurred.
FIG. 5.—Bony ankylosis and arrested disease less than two years after operation.

into the ilium and a tunnel prepared for the graft. The graft is driven home and the great trochanter replaced over the external end of the graft. Plaster of Paris is applied. No hæmorrhage and very little shock have been encountered in this operation. No plasma infusion or blood transfusion has been necessary following it.

I am grateful to Mr. S. L. Higgs for guidance in developing this operative technique for tuberculous hips. The following table shows the results of this operation, and includes also 4 cases of osteotomy with ischio-femoral graft.

TABLE II.—DISPLACEMENT OSTEOTOMY WITH GRAFT. RESULT OF 12 CASES ONE YEAR OR MORE AFTER OPERATION—TWO PATIENTS STILL WEARING HIP SPLINTS

	Firm ankylosis—stable hip		Unstable hip
	Bone	Fibrous	Fibrous
Osteotomy with graft along upper surface of neck..	5	1	2 (doubtful stability)
Osteotomy with ischio-femoral graft	2	2	0

Finally attention is drawn to the use of osteotomy to promote healing of active tuberculous disease in the hip. Three osteotomies with displacement were performed for patients with active disease, one in an adult, two in children. Osteotomies without displacement were performed for five patients, two of whom were adults and three children. In two of these cases a tuberculous focus in the upper end of the femoral shaft was also curetted. Two of the cases treated by osteotomy and a graft had active disease. In the case of adults these osteotomies were performed rather earlier than in the case of children, but the majority had had a year or more of preliminary conservative treatment. It was possible to discharge the majority of these patients ambulant, about four months after osteotomy; it was necessary to provide them with a well-moulded celluloid hip splint. An example of osteotomy for active disease is seen in the films of D. S. (figs. 6, 7 and 8).

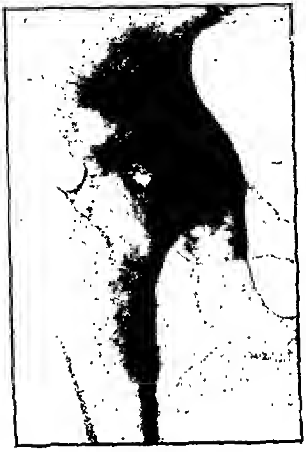


FIG. 6.

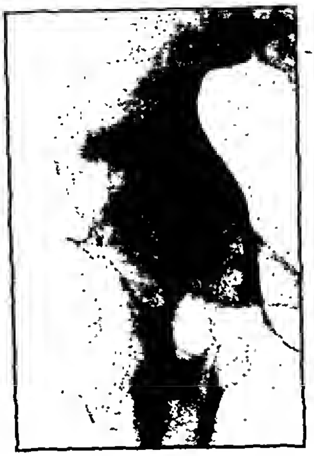


FIG. 7.

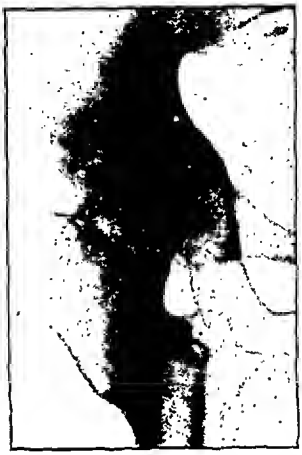


FIG. 8.

D. S., male. FIG. 6.—Case of active tuberculosis of the hip with gradually progressive acetabular disease of sluggish type.

FIG. 7.—Displacement osteotomy after three months' conservative treatment. Acetabular disease beginning to heal. Patient ambulant in celluloid splint.

FIG. 8.—Eighteen months after operation. Disease healed. Hip stable. No splint worn.

Some Points About the Monteggia Fracture

By W. SAYLE CREER, F.R.C.S.

THERE does not appear to be any accepted line of treatment for this awkward fracture, possibly because it is not common enough to provide any one surgeon with a very large series. Only 12 patients out of a total of 20,000 fracture cases seen at my clinics in the past ten years have had a Monteggia fracture.

The chief problem of conservative treatment has been to maintain reduction of the radial head when a good position of the ulna fracture was secured, and vice versa. The management of a number of cases has been simplified by open reduction and internal fixation of the ulna. However, conservative treatment frequently fails to obtain (or to maintain) reduction of the radial head although the ulna is in good position. In such cases late symptoms of pain and difficulty of using the elbow are a constant complaint.

Reconstruction of the orbicular ligament has been urged as a *sine qua non* for this element of the fracture, but any surgeon who has performed it readily appreciates the technical difficulty. Any form of early operation has been condemned because of the dangers of cross-union and of radio-humeral ankylosis. My limited experience is that early operation is not only essential but *per se* carries no such risk.

Of the 12 cases 8 were of the extension type (head of radius forwards), 3 of the flexion type and 1 not stated in the notes. 5 were treated personally and, because of the complaints of those treated conservatively, were submitted to surgery.

In 2 adults internal fixation of the ulna was effected by the passage of a Kirschner wire down the medullary cavity from the tip of the olecranon. The third case was a child and the fracture was in good position and required no internal fixation. On exposing the head of the radius in all 3 cases it was found that the bone had pierced the capsule of the elbow, was tightly gripped by it and was prevented from returning to its normal position by nothing but this structure. In the child although the radial head was displaced forwards the rent was situated posteriorly. No repair of the orbicular ligament was undertaken in any of the cases; but no instability ensued. There was no ankylosis, circum-radial ossification or myositis ossificans.

One case was operated on late—a boy of 5 who was seen six weeks after injury. The fractured ulna had united in good position, but the head of the radius was displaced outwards. There was an associated radial nerve palsy, which recovered with the usual splintage and physiotherapy. Six months after the accident open reduction of the radial head was carried out. Once again the bone was found to have pierced the joint capsule. In this case it might have been wiser to explore and attempt to repair or replace the orbicular ligament for, although the radial head appeared to be stable after suture of the muscles, it is now, four years later, unstable and displaced anteriorly. Elbow movements are only 70 degrees to 140 degrees, with pronation 30 degrees and supination 60 degrees. The boy and his parents think the result is good.

Another method of treating it would have been to excise the radial head. This was done four months after injury in a case treated conservatively elsewhere. The result has been extremely satisfactory for his only disability is the loss of 5 degrees of extension.

Early operation was followed by cross-union in one case. This was a man of 47 who was kicked by a horse and suffered a fracture of the extension type. Eight days later the ulna was reduced and fixed by a plate through one incision, and the head of the radius reduced through a separate one. As in the other cases the head of the radius had passed through a rent in the capsule and, when brought back into the joint, was stable. This man developed cross-union of radius and ulna. It is difficult to decide whether the cross-union should be ascribed to the operation or to the trauma. A kick from a horse on the forearm is probably as severe in its effects on the soft tissues as when a motor cycle rider suffers a compound fracture of the tibia due to direct violence. The cross-union may have resulted from a widespread hæmatoma due to the primary injury.

The "boutonnière" dislocation, especially of the thumb and at the shoulder, is well known to orthopædic surgeons as an indication for open reduction, but appears to have been overlooked in the management of the Monteggia fracture. Difficulty of reduction of any joint dislocation should always suggest this type of capsular tear and is a strong indication for early recourse to surgery. The alleged dangers of permanent stiffness consequent on early open reduction have probably been exaggerated. The following case of a postero-lateral dislocation of the elbow without fracture in a man of 45 is an example of a good result following early surgery. Three attempts at reduction by my registrar failed. Sixteen days after injury open reduction revealed that the whole of the lower end of the humerus had passed through a rent in the front of the joint capsule. The opening was enlarged and reduction revealed that the whole of the lower end of the humerus had passed 30 degrees of movement from the fully straight position was possible afterwards although he was still anæsthetized; but twelve months later he has elbow movement from 70 degrees to 180 degrees, 40 degrees of pronation and full supination, and X-rays show ligamentous ossification no more extensive than seen after every case of dislocated elbow.

Conclusions from these twelve cases of Monteggia fracture: (1) Open reduction of the radial head is frequently necessary—the "boutonnière" rent bars reduction. Repair of the orbicular ligament in the early cases does not seem essential. (2) Internal fixation of the ulna may be needed. (3) For the late case excision of the unreduced radial head gives a good result. (4) The danger of radio-humeral ankylosis or myositis ossificans consequent on early operation has been given undue prominence.

Section of Dermatology

President: SYDNEY THOMSON, M.D.

[*November* 21, 1946]

Ulcer of Vulva in Young Girl.—M. MOORE WHITE, M.D. (*By kind permission and in conjunction with* R. T. BRAIN, F.R.C.P.).

M. R., aged 17, was first seen on August 2, 1945, with an ulcer involving the right labium major and minor. She gave a history of ulcers in the mouth since the age of 3 and small ulcers on the vulva during the previous year which had healed without treatment. The amount of œdema present had varied as also the appearance of tender nodular areas adjoining the ulcer and posteriorly on the opposite labia. There was no history of vaginal discharge. Menstruation was regular except for a short time after admission. Katamenia at 14. Nothing relevant in past history. Strong family history of rheumatism. The girl was well-built and of healthy appearance. There were several red ulcers on the inner side of the cheek and lower lip. The fauces were not injected. An ulcerated area 2 in. × 1 in. involved the right labium minor and major posteriorly. It possessed a central slough and a hyperæmic edge, with some surrounding œdema. The ulcer was tender to touch. She was virgo intacta. There was no vaginal discharge. She had mild pyrexia for five days and for a short similar period later.

Wassermann, Kahn and gonococcal complement-fixation tests were negative. Subsequently the parents and a brother underwent the routine tests for venereal infection, which were all negative. The blood-count was normal. The E.S.R. was raised and has varied between 39 and 42 mm. fall in one hour (Wintrobe method).

A direct film from the ulcers in the mouth showed mixed organisms, fusiform bacilli and a few spirochætes. Culture: *Staphylococcus aureus, Streptococcus viridans* and *N. catarrhalis.* A direct film from the vulval ulcer showed Gram-positive and negative rods, and Gram-positive cocci and diplococci. Culture: *Staphylococcus aureus* (coagulase-positive and moderately penicillin-sensitive) and *Staphylococcus albus.* Frei-Hoffmann test was negative. No Donovan bodies were found. Tuberculosis, diphtheria and anaerobic infection were excluded. A biopsy was taken in September 1945. The report stated that the section showed delicate fibrous tissue thickly infiltrated with lymphocytes, plasma cells, macrophages and a few polymorphonuclear cells.

Dr. M. Löwenberg reported on a section taken in November 1945 that "diplococci, isolated and in groups and placed both extra- and intra-cellularly were present, which were not unlike gonococci in situation and in staining properties.... They resembled the gonococci found in prostatic and cervical lesions of long-standing, rather than the organisms found in recent mucosal lesions, since they were somewhat decreased in size and the Gram stain gave unreliable results, in that in the same section some diplococci were stained and others discoloured. They were best shown with Unna's polychrome methylene-blue; with this stain they showed the characteristic dark blue colour". He considered characteristic of a gonococcal lesion the presence of vesicles in the section, absence of elastic tissue and intracellular œdema.

A more recent biopsy, October 1946, reported chronic ulceration with no characteristic appearance of a gonococcal infection and no organisms present.

All tests for venereal disease were negative. Tests were later repeated and found negative by Dr. M. Shaw at the Royal Free Hospital who commented that the ulcer did not conform to those typical of venereal disease. She had seen one of a similar nature due to *B. crassus*, Döderlein's bacillus.

Local treatments include triple dye, various sulphonamide preparations, penicillin, propamidine, zinc peroxide, X-rays (one application only, 100 *r*).

The general treatments include administration of vitamins A, B, C and D in large doses. Course of N.A.B. 4·5 grammes. Sulphonamides, systemic penicillin 1,700,000 units. T.A.B. and gonococcal vaccines. Stilbœstrol.

My thanks are due to Dr. R. T. Brain, Dr. Mary Michael Shaw and Dr. Elizabeth Hunt for their help and advice with regard to this case and to Professor Webb for the numerous investigations and reports undertaken by his Pathology Department at the Three Counties Emergency Hospital and at the Royal Free Hospital.

Comment.—The girl was 15½ when admitted. She was not interested in the opposite sex, so that if the lesion were gonococcal it must have been innocently contracted. Gram-positive and Gram-negative diplococci have been isolated from the vulval smear on several occasions but have never been found intracellularly. Dr. Löwenberg, however, was able to isolate an intracellular diplococcus from a biopsy section which he demonstrated to Dr. Brain and myself. The organism stained deeply with Unna's polychrome methylene-blue, with Gram stain some took the stain, some appeared discoloured only. According to Dr. Löwenberg the section showed other morphological features characteristic of a gonococcal infection—notably vesicle formation in the epidermis, absence of elastic tissue and cellular infiltration more marked in the deeper layers.

Had the lesion been gonococcal one would have expected some response to penicillin, sulphonamides, T.A.B. and gonococcal vaccine.

It has been suggested by Dr. Hunt that the lesion resembles those observed in cases of erythema multiforme. The association with ulcers of the mouth, the history of recurrence, the presence of painful nodular areas adjoining the ulcer on the vulva from time to time, and the rheumatic family history support this diagnosis.

The possibility of dermatitis artefacta has been excluded.

Dr. R. T. Brain: I have observed this patient since 1945; her lesions are similar to those observed in other cases I have had in which bacteriological studies have failed to establish the ætiology of the condition and treatment has been of no avail. Since the patient started with small recurrent ulcers in the mouth and on the vulva one has to consider first of all the different varieties of recurrent ulcers. These can be classified as follows: (1) Aphthous ulcers which may be due to herpes simplex, monilia infections, or a group of obscure ætiology. These ulcers are usually small and recurrent, and healing is not usually delayed. (2) A rare condition called "*peri-adenitis mucosa necrotica recurrens*", as described by Sutton and others, usually beginning with firm subcutaneous nodules affecting the buccal or vulval mucosa. As a rule these ulcers are said to heal in a week or two, although sometimes they may persist for a year or longer. (3) Ulcus vulvæ acutum of Lipschutz is usually associated with infection with *B. crassus*, which, however, may not be of pathological significance, and in this case was not found. (4) Erythema multiforme bullosa may be followed by superficial ulceration, but the early eruptions do not present any difficulty and the subsequent ulceration is not commonly persistent.

The present case may now be regarded as presenting a chronic ulcer of the vulva and other conditions must be considered. (1) Tuberculosis usually produces a more deeply-coloured ulcer with undermined edges. The histology is fairly characteristic and tubercle bacilli may be found. In this case these findings were negative. (2) Actinomycosis would present a different clinical picture, and the organism was not found. (3) Tertiary syphilis has been excluded by blood tests and arsenotherapy. (4) Diphtheritic ulcers, the organism is usually found without difficulty. (5) Diphtheroid ulceration, in which the organisms are abundant although the pathogenicity of the diphtheroid bacillus is not generally accepted. (6) Ulcus molle, which was excluded because Ducrey's bacillus was not discovered, and, as in the next condition also, glandular involvement is a prominent feature. (7) Lymphogranuloma inguinale was excluded by tests with Frei's antigen as well as by the clinical picture. Finally, there are two conditions of chronic non-specific ulceration; namely, chronic simple ulcer of the vulva usually occurring with venereal infection in prostitutes, and phagedenic ulceration in which extending necrosis is more severe and progressive than in the present condition.

Dr. J. T. Ingram: Since Gram-negative organisms may be a cause of this condition I would suggest trying the effect of ½% parachlorophenol either alone or in penicillin cream.

Dr. J. E. M. Wigley; I favour the diagnosis of peri-adenitis mucosa necrotica. I have seen one or two cases affecting both the mouth and the vulva which have persisted for a number of years. One of them, I remember, was seen at intervals for six or seven years. The patient was always quite satisfied that the lesions of the mouth were healed by a very small dose of X-rays.

Dr. H. W. Barber: I was unable to examine this case properly, but I gather there has been recurrent ulceration of the mouth as well as of the vulva. The more likely diagnosis, I think, is that suggested by Dr. Wigley, which is the same condition as that described by Lipschutz.

When fully developed and unaltered by secondary infection, the ulcers, whether in the mouth or on the vulva, are distinctive, the circular raised and indurated border and the central plug resulting from necrosis being characteristic. I have never accepted Lipschutz' view that infection with *B. crassus* is responsible, and agree with Whitwell, G. P. B. (1934, *Brit. J. Derm.*, *46*, 414) that it is probably a virus disease.

As with herpes simplex, in females there seems sometimes to be a relationship with ovarian function, and the disease may begin for the first time at or after the menopause. In two such cases the ulcers ceased to appear after œstrogenic therapy was given over a period of some months. In younger women, as with herpes, the ulcers may occur chiefly just before the periods. In one case œstrogens given during the period and the first half of the intermenstrual period appeared to prevent involvement of the vulva, but the buccal ulcers continued, and they did not cease to form during pregnancy. In another case, however, complete remission followed such treatment.

I have recently seen my first case of the disease in which there were ocular symptoms—Behcet's syndrome. The patient is the wife of a medical man, and the eye condition was fully described to me by Mr. Savin. She is at present being treated with vaccinia virus.

Multiple Tuberculides, including the Scleroderma-like Form of Erythema Induratum.—H. W. Barber, M.B.

Mrs. F. B., aged 58.

Operations for tuberculous cervical adenitis at 9 and 12 years of age. In 1926 operations by Sir Harold Fairbank for tuberculous arthritis of the left shoulder-joint and tuberculosis of a metacarpal bone of the left hand. Four years ago operation for tuberculous ribs.

For twenty years she has been subject to recurrent attacks of erythema nodosum.

For about three years she has had recurrent nodules of erythema induratum, pigmented remains of which may be seen on the thighs and legs, and at her first visit to me (October 9, 1946) two of these nodules in the subsiding stage were present on the outer side of the right thigh.

The scleroderma-like areas on the right sole, inner side of the foot, and ankle, and on the inner side of the lower part of the left leg have been present for about two years.

In the past year, multiple patches of lichen scrofulosorum have appeared from time to time.

rather than the organisms found in recent mucosal lesions, since they were somewhat decreased in size and the Gram stain gave unreliable results, in that in the same section some diplococci were stained and others discoloured. They were best shown with Unna's polychrome methylene-blue; with this stain they showed the characteristic dark blue colour". He considered characteristic of a gonococcal lesion the presence of vesicles in the section, absence of elastic tissue and intracellular œdema.

A more recent biopsy, October 1946, reported chronic ulceration with no characteristic appearance of a gonococcal infection and no organisms present.

All tests for venereal disease were negative. Tests were later repeated and found negative by Dr. M. Shaw at the Royal Free Hospital who commented that the ulcer did not conform to those typical of venereal disease. She had seen one of a similar nature due to *B. crassus,* Döderlein's bacillus.

Local treatments include triple dye, various sulphonamide preparations, penicillin, propamidine, zinc peroxide, X-rays (one application only, 100 r).

The general treatments include administration of vitamins A, B, C and D in large doses. Course of N.A.B. 4·5 grammes. Sulphonamides, systemic penicillin 1,700,000 units. T.A.B. and gonococcal vaccines. Stilbœstrol.

My thanks are due to Dr. R. T. Brain, Dr. Mary Michael Shaw and Dr. Elizabeth Hunt for their help and advice with regard to this case and to Professor Webb for the numerous investigations and reports undertaken by his Pathology Department at the Three Counties Emergency Hospital and at the Royal Free Hospital.

Comment.—The girl was 15½ when admitted. She was not interested in the opposite sex, so that if the lesion were gonococcal it must have been innocently contracted. Gram-positive and Gram-negative diplococci have been isolated from the vulval smear on several occasions but have never been found intracellularly. Dr. Löwenberg, however, was able to isolate an intracellular diplococcus from a biopsy section which he demonstrated to Dr. Brain and myself. The organism stained deeply with Unna's polychrome methylene-blue, with Gram stain some took the stain, some appeared discoloured only. According to Dr. Löwenberg the section showed other morphological features characteristic of a gonococcal infection—notably vesicle formation in the epidermis, absence of elastic tissue and cellular infiltration more marked in the deeper layers.

Had the lesion been gonococcal one would have expected some response to penicillin, sulphonamides, T.A.B. and gonococcal vaccine.

It has been suggested by Dr. Hunt that the lesion resembles those observed in cases of erythema multiforme. The association with ulcers of the mouth, the history of recurrence, the presence of painful nodular areas adjoining the ulcer on the vulva from time to time, and the rheumatic family history support this diagnosis.

The possibility of dermatitis artefacta has been excluded.

Dr. R. T. Brain: I have observed this patient since 1945; her lesions are similar to those observed in other cases I have had in which bacteriological studies have failed to establish the ætiology of the condition and treatment has been of no avail. Since the patient started with small recurrent ulcers in the mouth and on the vulva one has to consider first of all the different varieties of recurrent ulcers. These can be classified as follows: (1) Aphthous ulcers which may be due to herpes simplex, monilia infections, or a group of obscure ætiology. These ulcers are usually small and recurrent, and healing is not usually delayed. (2) A rare condition called "peri-adenitis mucosa necrotica recurrens", as described by Sutton and others, usually beginning with firm subcutaneous nodules affecting the buccal or vulval mucosa. As a rule these ulcers are said to heal in a week or two, although sometimes they may persist for a year or longer. (3) Ulcus vulvæ acutum of Lipschutz is usually associated with infection with *B. crassus,* which, however, may not be of pathological significance, and in this case was not found. (4) Erythema multiforme bullosa may be followed by superficial ulceration, but the early eruptions do not present any difficulty and the subsequent ulceration is not commonly persistent.

The present case may now be regarded as presenting a chronic ulcer of the vulva and other conditions must be considered. (1) Tuberculosis usually produces a more deeply-coloured ulcer with undermined edges. The histology is fairly characteristic and tubercle bacilli may be found. In this case these findings were negative. (2) Actinomycosis would present a different clinical picture, and the organism was not found. (3) Tertiary syphilis has been excluded by blood tests and arsenotherapy. (4) Diphtheritic ulcers, the organism is usually found without difficulty. (5) Diphtheroid ulceration, in which the organisms are abundant although the pathogenicity of the diphtheroid bacillus is not generally accepted. (6) Ulcus molle, which was excluded because Ducrey's bacillus was not discovered, and, as in the next condition also, glandular involvement is a prominent feature. (7) Lymphogranuloma inguinale was excluded by tests with Frei's antigen as well as by the clinical picture. Finally, there are two conditions of chronic non-specific ulceration; namely, chronic simple ulcer of the vulva usually occurring with venereal infection in prostitutes, and phagedenic ulceration in which extending necrosis is more severe and progressive than in the present condition.

Dr. J. T. Ingram: Since Gram-negative organisms may be a cause of this condition I would suggest trying the effect of ½% parachlorophenol either alone or in penicillin cream.

Dr. J. E. M. Wigley; I favour the diagnosis of peri-adenitis mucosa necrotica. I have seen one or two cases affecting both the mouth and the vulva which have persisted for a number of years. One of them, I remember, was seen at intervals for six or seven years. The patient was always quite satisfied that the lesions of the mouth were healed by a very small dose of X-rays.

Dr. H. W. Barber: I was unable to examine this case properly, but I gather there has been recurrent ulceration of the mouth as well as of the vulva. The more likely diagnosis, I think, is that suggested by Dr. Wigley, which is the same condition as that described by Lipschutz.

When fully developed and unaltered by secondary infection, the ulcers, whether in the mouth or on the vulva, are distinctive, the circular raised and indurated border and the central plug resulting from necrosis being characteristic. I have never accepted Lipschutz' view that infection with *B. crassus* is responsible, and agree with Whitwell, G. P. B. (1934, *Brit. J. Derm.*, 46, 414) that it is probably a virus disease.

As with herpes simplex, in females there seems sometimes to be a relationship with ovarian function, and the disease may begin for the first time at or after the menopause. In two such cases the ulcers ceased to appear after œstrogenic therapy was given over a period of some months. In younger women, as with herpes, the ulcers may occur chiefly just before the periods. In one case œstrogens given during the period and the first half of the intermenstrual period appeared to prevent involvement of the vulva, but the buccal ulcers continued, and they did not cease to form during pregnancy. In another case, however, complete remission followed such treatment.

I have recently seen my first case of the disease in which there were ocular symptoms—Behcet's syndrome. The patient is the wife of a medical man, and the eye condition was fully described to me by Mr. Savin. She is at present being treated with vaccinia virus.

Multiple Tuberculides, including the Scleroderma-like Form of Erythema Induratum.—H. W. Barber, M.B.

Mrs. F. B., aged 58.

Operations for tuberculous cervical adenitis at 9 and 12 years of age. In 1926 operations by Sir Harold Fairbank for tuberculous arthritis of the left shoulder-joint and tuberculosis of a metacarpal bone of the left hand. Four years ago operation for tuberculous ribs.

For twenty years she has been subject to recurrent attacks of erythema nodosum.

For about three years she has had recurrent nodules of erythema induratum, pigmented remains of which may be seen on the thighs and legs, and at her first visit to me (October 9, 1946) two of these nodules in the subsiding stage were present on the outer side of the right thigh.

The scleroderma-like areas on the right sole, inner side of the foot, and ankle, and on the inner side of the lower part of the left leg have been present for about two years.

In the past year, multiple patches of lichen scrofulosorum have appeared from time to time.

The climacteric occurred at the age of 50 and she still has hot flushes. On the face and upper part of the neck are seen the pigmentation and telangiectasia described by Civatte, and usually known as "pigmented and reticular poikilodermia of the face and neck".

The patient is now in Nuffield House for investigation.

Blood-count.—Hypochromic anæmia (Hb 65%) with moderate anisocytosis and anisochromia. Polynucleosis without left shift.

B.S.R.—One-hour reading 56 mm.; two-hour reading 91 mm.

Films very streaky, indicating that B.S.R., after correction for anæmia, is markedly raised.

Urine: No abnormality except excess of indican.

Radiogram of chest: No evidence of disease of the lungs. Heart and mediastinal shadows are normal.

A Mantoux tuberculin test was made on November 16, 1946. There was no local reaction on November 18, but a typical eruption of erythema nodosum had occurred around the left knee, and was recognized by the patient as similar to those she had had periodically for twenty years.

A cutaneous test with tuberculin jelly was made on the right side of the back, and a control test on the left side (November 16, 1946). When examined on November 18, a typical outbreak of papules of lichen scrofulosorum had appeared on the site to which the tuberculin jelly was applied. Moreover a new patch of this eruption had occurred on the right thigh.

The most interesting lesions are the indurated plaques situated on the right sole, inner side of the right foot and ankle, and on the inner side of the left leg above the ankle. At the margins of the plaque on the right foot are raised, reddened nodules, extremely tender on pressure. The central part is white and hard, simulating morphœa. At points areas of necrosis have occurred with serous discharge.

The indurated plaque on the left leg is in part reddened on the surface, but palpation above it reveals extension of the induration, covered by normally coloured skin.

Exfoliative Erythrodermia with Marked Pigmentation.—J. E. M. WIGLEY, M.B.

E. R., male, aged 55.

History.—Dates from 1940 with the eruption apparently beginning on the right hand. In 1941-46 he attended St. Mary's Hospital as an out-patient from whence he was admitted to Paddington Hospital in May 1946 with a diagnosis of exfoliative dermatitis.

On examination.—At that time he had an almost universally red, slightly œdematous, scaling and much excoriated skin. There were a few weeping and bleeding areas, principally resulting from scratching. Irritation was very severe and difficult to control. The lymphatic glands in his neck, axillæ and groins were easily palpable. His liver and spleen were not palpable and general physical examination revealed no other abnormality. A blood-count at that time showed: R.B.C. 4,700,000; Hb 87%; C.I. 0·92; W.B.C. 32,000. Differential count: Polys. 61%, eosinos. 22%, lymphos. 10%, monos. 7%.

Since admission his progress has been variable. In June he had an attack of lobar pneumonia which responded to the usual treatment, and in October an attack of herpes zoster affecting the tenth dorsal segment on the right side. His skin has slowly lost its redness and become smooth, almost leathery, and appears stretched over his thorax. He has developed a remarkable brownish pigmentation which is almost universal, though it is noticeable that the area which was affected by the zoster is quite white. The irritation has almost ceased.

Numerous blood-counts have shown some variations from the normal. A moderate degree of lymphocytosis has been somewhat marked lately whilst there has been a fairly persistent eosinophilia. The following are examples:

	July 1	Aug. 12	Oct. 8	Nov. 15
W.B.C.	... 11,500	17,000	7,400	10,000
Polys.	... 52%	56%	58%	75%
Eosinos.	... 29%	25%	16%	3%
Lymphos.	... 16%	15%	22%	20%
Monos.	... 3%	4%	4%	2%

The Wassermann and Kahn tests are negative.

July 17: *Sternal puncture.*	N.	E.	B.
Polys.	43·5	5·5	—
Metamyelos.	4·5	1	—
Myelos.	12	10	0·5

Premyelocytes 2, myeloblasts 0, lymphocytes 2, monocytes 0, normoblasts 16·5, erythroblasts 2, megaloblasts 0·5.

Total nucleated cells—125,000 per c.mm. (normal 25,000—100,000).

Myeloid erythroblast ratio = 4·2 : 1 (normal) 8 : 1 to 2 : 1). B.P. 110/70.

Radiographic examination of his gastro-intestinal tract, made on account of his marked loss of weight, showed no evidence of neoplasm.

Urethane in 1 gramme doses t.d.s. seems to give a little relief and improvement.

Biopsy.—Skin: The epidermis is thickened and the superficial parts of the corium contain a marked increase of lymphoid cells, few reticulum cells and many eosinophils, situated chiefly around the blood-vessels, suggestive of a chronic lichenified dermatitis. There is really no evidence in the section alone to suggest a blood disorder.

Gland: The main feature of this lymphatic gland is severe active chronic inflammation. There are some granulomatous-looking areas which I cannot assign to any specific condition. They are rather better defined than one would expect in Hodgkin and more spindle-celled and less infiltrated than the examples we have of mycosis fungoides; this latter cannot be excluded, especially in view of the erythrodermia.

Comment.—The case is difficult to classify. It may yet develop into a leukæmia, and belong to the group of the reticulo-endothelioses. Addison's disease appears to be ruled out and no evidence of malignant disease was discovered. The patient looks ill though he persists in saying he feels better than he did on admission.

POSTSCRIPT.—Since the meeting his general condition has improved very much. His skin is still deeply pigmented.

Dr. A. C. Roxburgh: Is the pigment melanin?

Dr. Wigley: It was not remarked on in the section, but it is most likely melanin.

Dr. Brian Russell: In glandular biopsies on males, of between 60 and 70, with exfoliative erythroderma, Dr. Robb-Smith reports that he finds characteristic reactive changes of marked proliferation of histiocytes in the sinuses and also in the perisinusoidal tissue with many eosinophils and much melanin, a condition described by French as lipo-melanic reticulosis.

Dr. F. Parkes Weber: This slaty pigmentation makes me think of the possibility of argyria. An attempt at spectrographic diagnosis might be worth while.

Dr. Wigley: I thank Dr. Parkes Weber for his suggestion. The question of the pigmentation being the result of the ingestion or use of silver was thought of but the evidence did not support this at all.

The climacteric occurred at the age of 50 and she still has hot flushes. On the face and upper part of the neck are seen the pigmentation and telangiectasia described by Civatte, and usually known as "pigmented and reticular poikilodermia of the face and neck".

The patient is now in Nuffield House for investigation.

Blood-count.—Hypochromic anæmia (Hb 65%) with moderate anisocytosis and anisochromia. Polynucleosis without left shift.

B.S.R.—One-hour reading 56 mm.; two-hour reading 91 mm.

Films very streaky, indicating that B.S.R., after correction for anæmia, is markedly raised.

Urine: No abnormality except excess of indican.

Radiogram of chest: No evidence of disease of the lungs. Heart and mediastinal shadows are normal.

A Mantoux tuberculin test was made on November 16, 1946. There was no local reaction on November 18, but a typical eruption of erythema nodosum had occurred around the left knee, and was recognized by the patient as similar to those she had had periodically for twenty years.

A cutaneous test with tuberculin jelly was made on the right side of the back, and a control test on the left side (November 16, 1946). When examined on November 18, a typical outbreak of papules of lichen scrofulosorum had appeared on the site to which the tuberculin jelly was applied. Moreover a new patch of this eruption had occurred on the right thigh.

The most interesting lesions are the indurated plaques situated on the right sole, inner side of the right foot and ankle, and on the inner side of the left leg above the ankle. At the margins of the plaque on the right foot are raised, reddened nodules, extremely tender on pressure. The central part is white and hard, simulating morphœa. At points areas of necrosis have occurred with serous discharge.

The indurated plaque on the left leg is in part reddened on the surface, but palpation above it reveals extension of the induration, covered by normally coloured skin.

Exfoliative Erythrodermia with Marked Pigmentation.—J. E. M. WIGLEY, M.B.

E. R., male, aged 55.

History.—Dates from 1940 with the eruption apparently beginning on the right hand. In 1941-46 he attended St. Mary's Hospital as an out-patient from whence he was admitted to Paddington Hospital in May 1946 with a diagnosis of exfoliative dermatitis.

On examination.—At that time he had an almost universally red, slightly œdematous, scaling and much excoriated skin. There were a few weeping and bleeding areas, principally resulting from scratching. Irritation was very severe and difficult to control. The lymphatic glands in his neck, axillæ and groins were easily palpable. His liver and spleen were not palpable and general physical examination revealed no other abnormality. A blood-count at that time showed: R.B.C. 4,700,000; Hb 87%; C.I. 0·92; W.B.C. 32,000. Differential count: Polys. 61%, eosinos. 22%, lymphos. 10%, monos. 7%.

Since admission his progress has been variable. In June he had an attack of lobar pneumonia which responded to the usual treatment, and in October an attack of herpes zoster affecting the tenth dorsal segment on the right side. His skin has slowly lost its redness and become smooth, almost leathery, and appears stretched

Leiomyoma Cutis.—G. B. MITCHELL-HEGGS, O.B.E., F.R.C.P., and M. H. SMALL, M.R.C.S., L.R.C.P.

Miss D. C., aged 43.

Nodules first appeared on the right forearm in 1928, and have gradually become more numerous, although the original ones have not increased in size to any marked degree. When the skin is warm the nodules take on a red appearance, and are white when the skin is cool.

Present appearance.—The eruption is distributed over the forearms, face and neck, and there are a few nodules on the chest, abdomen and thighs. There are pink raised lesions; some papular, others nodular; some being elongated. The nodules are about the size of a half pea. The surface is smooth and glistening. There are no scales. On palpation they are of a firm consistence, almost rubbery. There is no tenderness. At first sight, the condition was thought to be sarcoidosis. The small nævoid nodules on the face first made their appearance about a year ago.

Past history.—1927: Bronchopneumonia. 1928: Burns of chest, with much scarring but no keloid formation. 1933: Erysipelas of face. 1939: Panhysterectomy and appendicectomy.

Family history.—Mother alive and well. Father died of pneumonia, 1906. Three sisters alive and well.

Investigations.—W.R. negative. Biopsy and section: Typical leiomyoma cutis. X-ray report: No abnormality detected in chest, hands or feet.

Erythrodermia in Lymphatic Leukæmia. (Malignant Erythrodermia).—G. B. MITCHELL-HEGGS, O.B.E., F.R.C.P., H. CORSI, F.R.C.S., and K. D. CROW, M.R.C.P.

F. W., 79 years, very deaf man.

The condition started with generalized pruritus seventeen months ago. One year ago generalized erythrodermia with fine, branny scaling and intense burning, which lasted for three months. Remission, with subsiding scaling and erythrodermia, but continued pruritus, lasted for nine months. Enlarged, painless glands appeared in the neck, axillæ and groins. Three months ago erythrodermia recurred, rather worse, with larger and more extensive scaling, and considerable enlargement of cervical and inguinal glands, as well as in the axillæ. Two months ago ectropion with epiphora developed and the patient complained of his "skin being too tight". Neuralgic pains in the right side of the head were only relieved by morphia.

Blood-count.—W.B.C. 26,400: polys. 8,448, lymphos. 16,368, monos. 1,320, eosinos. 264 per c.mm.

The skin is now universally red, especially over the head, neck and trunk, is covered with fine scales, and is diffusely thickened. All lymph glands are enlarged, most conspicuously the inguinal ones. The mouth and the nails are normal, spleen not enlarged, but liver is easily palpable. X-ray of the chest showed left ventricular hypertrophy, and generalized bronchitis, but no hilar node enlargement. Barium meal, on account of abdominal pain and constipation, showed nothing abnormal.

Treatment.—Radiotherapy, and arsenic by mouth, have caused the glands to diminish in size, and relieved the pain and pruritus considerably.

Hæmatology and Pathology.—(Dr. E. NEUMARK.)

Hæmatologically and histopathologically this case is one of lymphatic leukæmia.

Impetigo Herpetiformis. ? Pemphigus Vegetans.—J. E. M. Wigley, M.B.

P. B., male, aged 56.

History.—The eruption first appeared in May 1946 on the left calf as a white bleb surrounded by smaller spots. Fresh areas appeared over the leg, extending to the other leg, to the trunk, shoulder region, and the face. There has been some irritation, not at any time severe, and his general health has remained good. There is no history of asthma, hay-fever, or skin disease in his family. His work does not entail any special industrial risks.

On admission to hospital in August he presented a remarkable picture. The lesions were roughly of two types: the more numerous ones consisted of a round, roughened, and crusted area varying in size from ¾ to 1½ inches with concentric, incomplete rings of pustules and minor blisters containing purulent fluid surrounding it. On each shoulder, spreading to the sides of the neck, were considerable areas of reddened skin surrounded by an irregular margin of similar pustules and small blisters. Over the whole of these surfaces were irregular lines of purulent blisters giving an almost lattice-work appearance. The background of both types of lesion showed varying degrees of pigmentation which appeared to darken in colour as the blisters faded away. To-day the areas on the shoulders are represented by pigmentation only. It is noticeable that the anogenital region and the mouth are not affected.

Cultures from the blisters revealed *B. coli* on one occasion and a mixture of *Staphylococcus aureus* and hæmolytic streptococci on more than one occasion.

Treatment.—External application of penicillin cream produced no change and a course of 125,000 units of systemic penicillin was ineffective. Since September he has been taking sulphadiazine, 1 gramme per day, and there appears to be slow but definite improvement in his condition.

I have not seen a clinical picture quite like this before but the lesions reminded me strongly of some coloured illustrations in one of the older dermatological atlases in which the name of the condition was given as impetigo herpetiformis. It also seems to fit in with the description of that condition given in Ormsby and Montgomery's "Diseases of the skin," 1943. The condition was originally described by Hebra in 1872 and subsequently by various other authors. Although more frequently seen during pregnancy it has also been reported in non-pregnant males, as in this case.

I shall be interested to see if this case will develop into a true pemphigus vegetans.

Dr. L. Forman: I have seen two similar cases, commencing with vegetative lesions on the scalp and both regarded as pemphigus vegetans. In each case superficial ulceration developed in the mouth mimicking secondary specific mucous patches. Large vegetating plaques developed in the flexures of the armpits and groins, and over the trunk. One case has cleared completely after eighteen months in hospital and has remained well for five months. The other patient made considerable improvement in about the same time.

Papulo-Necrotic Tuberculides.—Louis Forman, M.D.

R. G., male, aged 13 years.

1943, tuberculous glands removed. Operation followed by pericardial effusion. Rash appeared May 1946, cleared, but relapsed October 1946.

X-ray chest negative.

The boy shows Fröhlich's adiposity; right testicle not palpable. There is a very profuse eruption over arms, buttocks and thighs, of small red papules, vesicular, pustular and necrotic. Over the back there are grouped, skin-coloured papules of lichen scrofulosorum. Small pitted scars are seen over limbs and face. Tuberculin jelly patch test strongly positive, the reaction being a grouped papular one, mimicking the lichen scrofulosorum already present.

I have one case of leukæmia alive and well after six years, so that long remissions at least are not unknown.

Dr. Mitchell-Heggs: This man complained of very severe neuralgia of uncertain origin. It resisted all ordinary treatment, but as soon as the X-ray treatment of the glands made itself felt and the glands began to get smaller, the pain disappeared.

? Epidermodysplasia of Lewandowski and Lutz. ? Abortive Form of Blastomycosis or Chromoblastomycosis.— H. W. Allen, D.M.

G. M., butcher and farmer, aged 59 years, came to see me first in July for a warty condition of his hands. The condition is not hereditary. There is no consanguinity of parents. His previous history included slight rheumatism of the upper limbs and slight patches of pityriasic dermatitis of scalp. The present trouble started as warts, which never caused irritation.

On examination.—The clinical picture was not that of a verrucose blastomycosis or chromomycosis, and certainly not that of verrucæ vulgares. The distinguishing characteristics were those of epidermodysplasia verruciformis, i.e. very small warty lesions, often flat-topped, occasionally grouped, chiefly affecting the hands symmetrically, but differed in that the dorsum of the hand was not affected as is usual, and by the characteristic minute brown ring which could be shown on diascopy to outline a lesion sharply.

Scraping of the lower layers followed by teasing out in saline enabled me to demonstrate the mycelium and double-contoured occasionally brownish cells of a blastomyces or zymonema.

Culture gave a perfect white fluffy growth, which from previous experience, and by reference to illustrations in Sutton's textbook, I should classify as a blastomyces.

The culture has disappeared, and, as anticipated, X-ray treatment has made it impossible to repeat it.

Treatment.—I asked Dr. Charles Wroth of Exeter kindly to give ¾ B (i.e. ¾ pastille dose) at the earliest possible moment. As a result there was improvement; he gave prolonged treatment, and wrote on October 25 that "the skin condition of the hands and wrists has cleared up satisfactorily, but the numerous minute nodules of hard skin (? warts) although smaller, have not completely disappeared". Prolonged X-ray treatment has failed to clear up the condition.

It is regrettable that no biopsy was obtained at the first visit, particularly as it is possible that X-ray therapy has permanently affected the characteristic microscopic structure.

Dr. J. E. M. Wigley: I should have thought lichen planus was the most likely diagnosis here.

Dr. F. Parkes Weber: I must say that I have not seen the original account by Lewandowski and Lutz, but, judging by the name, "epidermodysplasia verruciformis", this case must be vastly different from what they described under that heading. The patient is 59 years old, and if he has only just begun to have the disease—for the last half-year, I think he told me—it would be rather late in life to develop a dysplasia. I think that Dr. Wigley's diagnosis holds the field.

Dr. A. C. Roxburgh: I support the diagnosis of lichen planus.

A Hereditary Ectodermal Dysplasia, Hitherto Not Described, Including Grouped Comedones.—C. H. Whittle, M.D.

D. B., a married woman, aged 40.

The patient has had this thick rather dry skin and grouped comedones since puberty. They are most noticeable at the root of the nose, in the naso-labial folds, on the chin, on the shoulders, in the axillæ, on the breasts, in the groins, in the bends of the elbows, on the fronts of the knees. There is one cutaneous horn on the left cheek.

In all essentials it resembles the cases of Panton and Sequeira (*Quart. J. Med.* (1925), **18,** 250), MacCormac and Whitby (*Proc. R. Soc. Med.* (1936), **30,** 192), MacCormac (*Proc. R. Soc. Med.* (1928), **21,** 1171) and other authors.

Blood-count (7.11.46).—R.B.C. 4,100,000 per c.mm.; Hb 80% (12 grammes); C.I. 1; mean cell diameter (halometer) 7·1 μ; W.B.C. 28,000 per c.mm. Polys. 31% (8,100 per c.mm.), lymphoid cells 67% (18,700 per c.mm.), mononuclears 2% (560 per c.mm.). The predominating cell was the mature-looking, small lymphocyte. Some cells were very large and primitive-looking, and contained a number of nucleoli, their cytoplasm being mainly basophilic, sometimes vacuolated and with pseudopodic processes. Numerous mitotic figures were seen which were mainly atypical in shape, a most unusual phenomenon in lymphoid cells. Supravital preparations with neutral red and Janus green showed most cells to be non-motile and non-granular, confirming their lymphoid character.

Sternal marrow examinations showed 75% of the cells to be lymphoid, the normal being 5% to 20%, but basket cells were not prominent in either blood or marrow films.

Pieces of skin examined histologically showed some parakeratosis, little hyperkeratosis, and some spongiosis. The lymphatic infiltration extends into the superficial layer of the epithelium. There are many melanophores and many giant cells, which appear to destroy the elastic. The elastic fibres in the intermediate zone stain badly and are coarsened throughout, resembling those seen in pseudoxanthoma elasticum.

A gland excised from the right groin did not present the usual follicular pattern, but consisted of sheets of cells, staining darkly, with round nuclei. The glandular capsule is infiltrated and, in places also, the sinuses. There are many large reticulum cells. The appearances are those of lymphatic leukæmia.

Diagnosis in this case is based on clinical grounds ("homme rouge"), glandular enlargement, &c., and on the blood findings confirmed by sternal marrow biopsy, and on the histology of the skin and of a lymph gland.

Dr. J. E. M. Wigley: I think there is a relatively small group of cases which can be recognized clinically and which were described by Sequeira and Panton (*Brit. J. Derm.* (1921) 33, 291) under the term of "lymphoblastic erythroderma". In these cases the skin presents a peculiar, dull, red-brick colour and a definite thickening to palpation, part at least of which is the result of cutaneous œdema. There is usually generalized enlargement of the lymphatic glands and very marked irritation. The blood-counts vary immensely, even from week to week, and one week there may be a small leucocytosis whilst in the following week the leucocytosis may be considerable. Almost invariably there is considerable relative lymphocytosis. I saw one of Sequeira's original cases in 1921 and have only seen two or three such clinical pictures since. The present case appears to me to present the clinical picture which I have tried to describe.

Dr. Brian Russell: I have a woman under observation with an identical skin appearance and a white cell count of 24,000 per c.mm., 83% of which are lymphocytes.

Dr. C. H. Whittle: The point which has interested me most is whether any of these leukæmic erythrodermia cases recover. Once the diagnosis of leukæmia is made the death warrant is more or less signed. Yet on going through the reports in the American literature I find that this is not necessarily true, and I can recall one case (Fraser, J. F., *Arch. Derm. Syph.* (1943) 48, 42), clinically lymphatic leukæmia, with a leucocytosis as high as 100,000 per c.mm., 80% lymphocytes (somewhat resembling monocytes) which showed complete recovery following X-ray therapy for at least two years. Sternal marrow was negative.

On the other hand a careful study of a case of erythrodermia of seven years' history, clinically leukæmic, by Hitch, J. C., and Smith, Dudley C. (1937) *Arch. Derm. Syph.*, 36, 1, with counts of 30,000 to 40,000 leucocytes, 80% to 90% lymphocytes, showed no histological evidence at autopsy of leukæmia. Either leukæmia is a disease from which recovery is possible, though infrequent, or many of these erythrodermia cases are not true leukæmias (Hugh-Jones, P., and Whittle, C. H., *Proc. R. Soc. Med.* (1943) 36, 612). The subsequent history of such cases with histological study is vital for their proper assessment.

mation with œdema and purulent infiltration in papillary layer of corium. Gram-stains show no bacteria. There are no special features suggesting virus infection.

Drugs.—No bromides or *iodides* have been given. The following were used by the home doctor:

(1) Belladonna—for a day or two only, 23.9.46.

(2) Cough mixture from 23.9.46 to 14.10.46

containing Vin. Ipecac.
Tr. Scillæ
Syr. Tamarinth
Syr. Rhœados
Syr. Ribis nig.

(3) Glyc. of ichthyol for balanitis, 27.9.46.

(4) Plain tulle-gras for the burn, followed by penicillin cream. Tulle-gras contains 1% balsam of Peru which itself contains benzyl benzoate and other similar substances.

Wassermann negative.

Mantoux 1 : 1,000 negative, human and bovine.

Comment.—Virus disease or drug eruption, ? ipecacuanha.

Dr. J. E. M. Wigley: I would suggest that it might be simpler to give this child small doses of whatever drugs are found to have been present in the cough mixture, one at a time. The result should prove most helpful, but I still think the clinical appearances of the eruption are strongly in favour of it being a bromide one.

Dr. F. Parkes Weber: Much depends on the course of this eruption. If the eruption now disappears completely without any special treatment, I think that one must regard it as having been a bromide eruption. But to make quite sure of this, the child (as suggested) might be given a little bromide cautiously to see if the eruption returns and if the child has an idiosyncrasy towards bromide. With care it would not do the child any harm.

Dr. Whittle: I questioned the mother very carefully and the doctor three times and got the whole list (given above) with the various ingredients of the cough mixture. Bromides were conspicuous by their absence.

POSTSCRIPT (23.12.46).—A course of bromide by mouth for a week followed by a course of iodide by mouth has *not* resulted in any further outbreak of the eruption.—C. H. W.

Lupus Vulgaris and Tuberculides of Face.—BERNARD GREEN, M.R.C.S., L.R.C.P.

Mrs. D. J. S., aged 63.

This patient first came under my care in September 1942, with a patch of lupus vulgaris affecting the side of the left cheek and the lobe of the left ear. I treated this in various ways, including acid nitrate of mercury and the disease was kept under control. In February 1946, with the advent of calciferol, I gave her high potency ostelin. This she continued to take for six months and the improvement, as you have seen, is dramatic. To-day there is little, if any, activity to be seen. In August 1946, whilst still taking calciferol, she developed a papular eruption on her face, mainly affecting the cheeks, forehead, chin and side of the nose. This I treated by exposure to ultraviolet light once a week, and some of the lesions have resolved, leaving depressed scars.

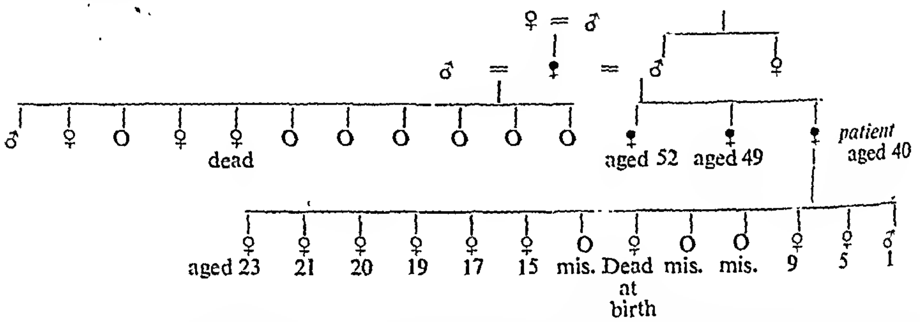
A skiagram of the chest revealed nothing abnormal. E.S.R. and blood-count showed no abnormality and a Mantoux test 1 : 10,000 is positive.

I show this case because I feel it is of some interest in view of the fact that whilst she was on calciferol treatment and the patch of lupus vulgaris was disappearing she developed these tuberculides. Whilst on calciferol treatment she felt depressed, heavy as though carrying a ton weight, had tachycardia and indigestion. All these symptoms have disappeared since stopping the calciferol treatment.

There has not been much change since puberty, but she noted some improvement in the condition after the first child was born and after each subsequent pregnancy. Her menstrual periods have been normal. She has nine children alive and well. She feels the cold but is not grossly myxœdematous in appearance.

Vitamin A.—Vitamin A in plasma 74 units (low normal); carotene in plasma 66 units (subnormal).

Family history.—Her mother and her only two sisters also show the same condition. None of her children do, even those, 6 in all, who have reached and passed puberty.



Dr. Whittle: I find difficulty in classifying this condition. The lesions include grouped comedones, but not such as are described by Thin, G. (1888) *Lancet* (ii), 712, Crocker, H. Radcliffe (1888) *Lancet* (ii), 813, and Wetherell and Sympson (1889) *Lancet* (i), 169. The skin is generally thick and abnormally dry. I should be grateful for suggestions.

Dr. F. Parkes Weber: Dr. Whittle has certainly proved his point, namely, that this is a form of family ectodermal dysplasia, although not so very many members of the family suffer from it. The hard follicular plugs (especially on the legs) constitute a striking feature, and I fancy that the condition is really not extremely uncommon. I would like to call it "a familial hyperplastic follicular dermatosis".

Dr. Whittle: I thank Dr. Parkes Weber for his suggestion. I will bear the title in mind.

? Kaposi's Varicelliform Eruption.—C. H. WHITTLE, M.D.

P. S., a boy, aged 1½ years.

History of an eruption starting about 30.9.46 on the left leg about a week after a burn, with blistering, of the left knee. The lesions increased in number and size and new ones appeared on the right leg, and a few small ones on the face. When first seen by me, 14.10.46, he presented large pyodermatous deep-red, heaped-up granulomata varying in size up to 2 cm. diameter on front and sides of legs chiefly below the knee. They grew larger—up to 3 to 4 cm. diameter—and the child was admitted to hospital for investigation.

Course.—His general health has been excellent throughout and his temperature never above 99°. The lesions have gradually subsided and there are now left the bluish-brown healing, or healed, areas visible on both legs. At one stage a few pock-like lesions were coming up about 8 mm. diameter, very reminiscent of smallpox pustules, with umbilication, but mostly the lesions were heaped pustular granulomata.

Bacteriology.—No organisms have been seen in, or grown from, the pus at any stage on repeated trials. Aerobic and anaerobic cultures have been put up, all sterile.

Animal inoculation.—Professor S. P. Bedson has kindly inoculated fluid from the pustules removed by sterile pipette before they were broken. Inoculations were made into mice intracerebrally, and guinea-pigs intradermally, with passage in the latter, but no virus of herpes or other type has been demonstrated.

Biopsy of pock-like lesion (section shown).—Non-specific granulomatous inflammation with œdema and purulent infiltration in papillary layer of corium. Gram-stains show no bacteria. There are no special features suggesting virus infection.

Drugs.—No bromides or *iodides* have been given. The following were used by the home doctor:

(1) Belladonna—for a day or two only, 23.9.46.

(2) Cough mixture from 23.9.46 to 14.10.46

containing Vin. Ipecac.
Tr. Scillæ
Syr. Tamarinth
Syr. Rhœados
Syr. Ribis nig.

(3) Glyc. of ichthyol for balanitis, 27.9.46.

(4) Plain tulle-gras for the burn, followed by penicillin cream. Tulle-gras contains 1% balsam of Peru which itself contains benzyl benzoate and other similar substances.

Wassermann negative.

Mantoux 1 : 1,000 negative, human and bovine.

Comment.—Virus disease or drug eruption, ? ipecacuanha.

Dr. J. E. M. Wigley: I would suggest that it might be simpler to give this child small doses of whatever drugs are found to have been present in the cough mixture, one at a time. The result should prove most helpful, but I still think the clinical appearances of the eruption are strongly in favour of it being a bromide one.

Dr. F. Parkes Weber: Much depends on the course of this eruption. If the eruption now disappears completely without any special treatment, I think that one must regard it as having been a bromide eruption. But to make quite sure of this, the child (as suggested) might be given a little bromide cautiously to see if the eruption returns and if the child has an idiosyncrasy towards bromide. With care it would not do the child any harm.

Dr. Whittle: I questioned the mother very carefully and the doctor three times and got the whole list (given above) with the various ingredients of the cough mixture. Bromides were conspicuous by their absence.

POSTSCRIPT (23.12.46).—A course of bromide by mouth for a week followed by a course of iodide by mouth has *not* resulted in any further outbreak of the eruption.—C. H. W.

Lupus Vulgaris and Tuberculides of Face.—BERNARD GREEN, M.R.C.S., L.R.C.P.

Mrs. D. J. S., aged 63.

This patient first came under my care in September 1942, with a patch of lupus vulgaris affecting the side of the left cheek and the lobe of the left ear. I treated this in various ways, including acid nitrate of mercury and the disease was kept under control. In February 1946, with the advent of calciferol, I gave her high potency ostelin. This she continued to take for six months and the improvement, as you have seen, is dramatic. To-day there is little, if any, activity to be seen. In August 1946, whilst still taking calciferol, she developed a papular eruption on her face, mainly affecting the cheeks, forehead, chin and side of the nose. This I treated by exposure to ultraviolet light once a week, and some of the lesions have resolved, leaving depressed scars.

A skiagram of the chest revealed nothing abnormal. E.S.R. and blood-count showed no abnormality and a Mantoux test 1 : 10,000 is positive.

I show this case because I feel it is of some interest in view of the fact that whilst she was on calciferol treatment and the patch of lupus vulgaris was disappearing she developed these tuberculides. Whilst on calciferol treatment she felt depressed, heavy as though carrying a ton weight, had tachycardia and indigestion. All these symptoms have disappeared since stopping the calciferol treatment.

Cutaneous Papillomatosis.—R. M. B. MacKenna, M.D., and Brian Russell, M.D.

Miss B. M., aged 50.

In May 1946 she complained of soreness and thickening of the skin in the right groin. This condition had been present in a much milder form for years previously. At the same time, she noticed spots on the calves which her doctor diagnosed as purpura.

In August 1946 she noticed many warty lesions on the limbs and in the axillæ. The condition in the right groin spread to the left side and to the anal and internatal regions.

Family history.—Nothing relevant discovered.

Past history.—She suffered from gastric neurosis in the 1914-18 war. For three years she has again suffered from dyspepsia and retrosternal pain after meals. She has been very strict with her diet, not taking any meat or vegetables for the last three years, her diet consisting only of eggs, when available, milk, and bread and butter, with occasional oranges.

On examination.—A well-nourished woman. No anæmia. No evidence of endocrine disturbance. Mild angular conjunctivitis. Scalp shows heavy *pityriasis*. Slight acne of front of chest and numerous de Morgan's spots. Numerous lesions resembling common warts on hands, forearms, and axillæ, some with brownish pigmentary changes, particularly in their bases which are infiltrated and raised in some lesions. In the groin flexures, particularly on the right side. there is a slate-brown verrucose and sodden condition of the skin: also in the internatal region and perianal region, and involving the gluteal fold, with numerous satellite warty lesions around, varying from pinhead size upwards. There is a similar condition involving the navel. Purpura is not now apparent.

Investigations.—Biopsies from right forearm and internatal region both show papillomata. Vitamin C saturation test within normal limits. Wassermann reaction negative. Scraping from pubic lesions showed no fungi and culture yields no growth of fungi. Breasts: No evidence of neoplasm.

Gynæcologist's report.—No pelvic abnormality discovered.

Blood-count within normal limits.

Catheter specimen of urine.—Centrifugalized deposit W.B.C. less than 1 per 1/6 in. field; R.B.C. less than 1 per 1/6 in. field: hyaline casts less than 1 per 2/3 in. field. Gram-stained film: No organisms. Culture sterile.

X-ray.—Chest: No evidence of pulmonary disease. Stomach and duodenum normal. Follow through: No neoplasm demonstrated in the alimentary tract.

Sigmoidoscopy: Nothing abnormal detected.

Treatment.—Treatment has consisted of three doses of X-rays 80 r each to vulva, anal area, and armpits; vitamin supplements, and bland local applications.

Comments.—This patient appears to be in good health apart from her skin condition, and full clinical and radiographic examination does not reveal the presence of a neoplasm. The histology of the biopsies performed is not that of acanthosis nigricans, as there is no increase of pigment in the basal and dendritic cells of the epidermis and there are no areas of atrophy in the prickle-cell layer; it is rather that of simple papillomata.

H. Gougerot and A. Carteaud ("Year Book of Dermatology and Syphilology", 1932, p. 174) tabulate four forms of cutaneous papillomatosis and differentiate them from epidermodysplasia verruciformis, verrucæ planæ juveniles and morbus Darier. It is suggested that this case resembles the type "pigmentées verruqueuses" of Gougerot, Clara and Bonnin. The patient is also a seborrhœic subject.

Dr. F. Parkes Weber: I think the condition of the umbilicus is of great importance in regard to diagnosis. In my view the involvement of the umbilical region does really suggest acanthosis nigricans.

[*December* 19, 1946]

Erythematous Initial Tuberculide

By W. J. Hohmann, M.D., Groningen, Holland

During the occupation in Holland conditions of health and nutrition were greatly depressed, though they were not so bad in the north-east of Holland, where I was living and made my observations, as they were in other parts of the country. In 1942 a case was sent to me by a practitioner who stated that he had never seen this peculiar type of eruption before and I, too, had to admit that I had not seen it before. The patient showed a rash consisting of erythematous flat papules with pin-point small vesicles here and there, located on the neck and the extensor sides of the forearms, accompanied by erythema nodosum and conjunctivitis phlyctenulosa. It was impossible to make a diagnosis but an atypical form of tuberculide was presumed and radiological changes in the lung were found. The Pirquet tuberculin test was bullous. Though the diagnosis "atypical tuberculide" did not satisfy me, it was impossible to classify the dermatosis under one of the existing forms of tuberculides.

Altogether I saw six of these cases, all showing radiological changes in the lungs with a high sensitivity of tuberculin. In Urbach's book on Allergy, I came across the publications of Christjansen, Geissler, Kojima, Keiser, on tuberculin exanthemata. They believed that when an incipient tuberculosis passes from the first phase of Ranke into the second, at the moment when tuberculin sensitivity is at its highest, the application of tuberculin can give rise to exanthematous reactions. The skin eruption I saw might possibly also indicate this moment. These six patients stated that they had never had tuberculosis, but it was impossible for me to exclude an earlier infection with certainty.

From these six patients I came to the tentative conclusion that this dermatosis (1) was not just an atypical tuberculide, but that it must be a *very typical* one; (2) had a transient character (the rash disappeared in a few days to two to three weeks); (3) in some cases had a slight resemblance to erythema multiforme Hebræ but was distinctly different in its evolution; (4) was accompanied by a high sensitivity to tuberculin; (5) was, most likely, connected with tuberculosis; (6) *possibly* indicated a primary infection.

In 1945 I saw two nurses who had been tested for Pirquet and Mantoux reactions with negative results a few months previously; and the X-ray examination was also negative. Now they showed the same skin rash, the sensitivity to tuberculin was very high, and the X-ray showed changes in the lungs, most probably a primary tuberculosis. Later on the diagnosis of pulmonary tuberculosis was easily confirmed.

The previous medical examination excluded in these two nurses an earlier tuberculous infection.

Therefore my conclusion became more definite, and No. 6 (above) became: *most likely* indicated a primary infection.

In the earlier literature on skin rash in tuberculosis, Uffenheimer, Kundratitz and von Moritz record a few cases of children with a primary tuberculous infection developing a transitory skin rash, in one case more or less similar to erythema multiforme Hebræ.

In the middle of 1945 a patient came to hospital with pneumonia and was given sulphathiazole and a fairly extensive rash appeared. When I examined the eruption in the light of this recent experience, I said at once that it must be primary tuberculosis. In ten days' time the rash disappeared and the temperature came down, but two weeks later the patient developed fever again, and she died of meningitis tuberculosa. Post-mortem examination showed a primary focus in the lung.

It was noted that in this case the high sensitivity to tuberculin decreased in a very short time to just slightly positive, which might be an indication that danger is ahead. I was therefore certain that the dermatosis indicates a primary infection.

Bloch[1] published a case which must be similar to my cases, under the title: "Atypical Tuberculide Resembling Erythema Multiforme." As he saw only one case, he could not connect it with primary tuberculosis.

In Darier's "Précis de Dermatologie", I found one interesting sentence: "Si l'on se trouve en présence d'un de ces cas, que les travaux du Prof. Landouzy et de ces élèves ont montrés d'être assez fréquents, où l'érythème polymorphe se développe à la faveur de la tuberculose, il y a lieu de prescrire aux convalescents une hygiène appropriée et de les soumettre à une surveillance prolongée."

As in those days erythema nodosum was included with erythema multiforme, I cannot make out to what symptoms Landouzy referred. In the French bibliography after the war, I also found a few cases. In the Swedish bibliography I saw the report of a case that ended fatally and post-mortem examination was performed. A primary focus in the lung was found (the case was published for a different reason).

Assuming that an idiopathic form of erythema multiforme Hebræ actually exists, I suggest that where a disease of known ætiology but resembling the skin eruption of that disease is described, it should be named in such a manner as to make evident the more marked characteristics.

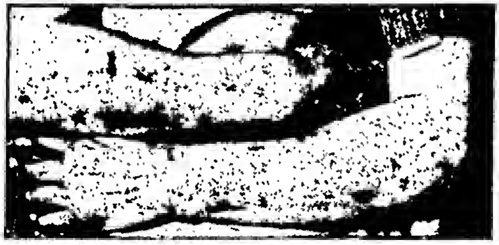


FIG 1.—Woman aged 60. Erythematous initial tuberculide.

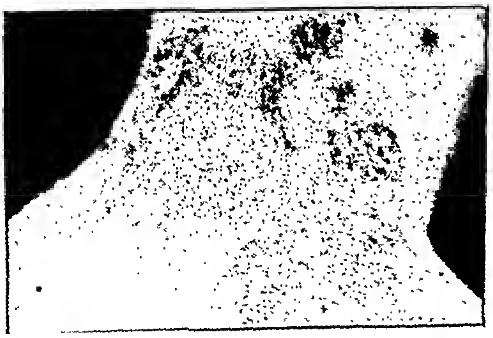


FIG. 2.—Woman aged 30. Erythematous initial tuberculide.

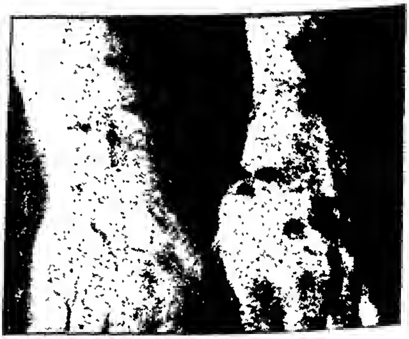


FIG. 3.—Woman aged 30; Erythematous initial tuberculide.

This dermatosis has some or all of the following characteristics:

(1) Rose-coloured to more livid patches, only slightly raised above the surface of the skin, with very little superficial infiltration; showing so little inflammatory œdema that the natural lines of the skin remain intact or are even more exaggerated; capricious of contour with a gradual change to the normal aspect of the skin and disappearing completely with diascopy; healing in a few days' to a few weeks' time whereby the efflorescence gets uniformly paler, and leaves no scars or pigmentation (*see* fig. 1).

---

[1] Bloch, B., *Schweiz. med. Wschr.* (1923) 53, 639.

(2) Pin-point, minute vesicles, on a red surface, rarely becoming confluent so as to form a bulla; showing a yellowish-brown transparent aspect and healing with fine scaling (*see* fig. 2).

(3) Spherical papules, pea-size, with a smooth glittering surface and flattened top, yellow to reddish-brown, showing practically no infiltration by diascopy and healing without scars.

(4) Nummular, flat, slightly elevated, red, œdematous papules without visible skin lines, and without deep-seated infiltration. When healing the rash gets paler and disappears. Very rarely a larger area of the skin may have this aspect (*see* fig. 3).

(5) Rounded or oval, bright red, tender nodes, later changing into dusky lividity losing their tenderness in this phase. The nodes undergo re-absorption, leaving behind a bluish hæmorrhagic discoloration which may change colour from blue to green and then to yellow before it disappears completely (erythema nodosum).

(6) The rash usually selects the extensor sides of the extremities, the neck and in some cases the face, *and is accompanied by some of the following symptoms*:

(*a*) A very high tuberculin sensitivity characteristic of the disease and essential for the diagnosis.
(*b*) Fever.
(*c*) General malaise.
(*d*) Enlarged hilus, or infiltration in the lung.
(*e*) Pleuritis.
(*f*) Conjunctivitis phlyctenulosa, or irritatio bulbi.

Furthermore

(1) Is transitory and does not recur.
(2) The skin eruption is harmless but prognosis must be guarded because
(3) it points with certainty to a primary tuberculous infection.
(4) The condition occurs at all ages.

I would suggest that this syndrome be called *tuberculosis initialis cutis erythematosæ* or *erythematous initial tuberculide*.

Dr. W. N. Goldsmith: Will Dr. Hohmann tell us more about the technique and results of the tuberculin tests?

Dr. Hohmann: I made a dilution of one to ten, one to one hundred and so on. I found a positive reaction even with a dilution of one to one hundred million. The reaction was adequate, that is to say, it was proportionate to the dilution employed. This is important, as in dermatoses resembling erythema multiforme Hebræ it is necessary to exclude an isomorphic Köbner effect, so common in this disease. Therefore it is always necessary to have controls.

Dr. Goldsmith: What was the subsequent history of most of these cases?

Dr. Hohmann: Some developed tuberculosis and some healed up; one case died. I do not think a certain prognosis is coupled to this eruption, it only makes possible the early diagnosis of primary tuberculosis about two months after the infection. On the other hand if a sudden decrease of the sensitivity to tuberculin in a short time is observed, this might be regarded as a fatal indication. All the cases of which I have been speaking had a very high sedimentation rate.

Dr. H. Corsi: We should all like to compliment Dr. Hohmann on his technique of presentation. He has not only spoken to us in admirable English, but has printed the words for us on the lantern screen. The combination of the spoken and the visible word has brought this subject very clearly before us.

The President: We have to thank Dr. Hohmann for a most interesting discourse—a subject excellently presented and certainly most stimulating of thought. We ask him to take back with him to Holland not only our thanks to himself but also our compliments to our Dutch colleagues.

very short time to just slightly positive, which might be an indication that danger is ahead. I was therefore certain that the dermatosis indicates a primary infection.

Bloch[1] published a case which must be similar to my cases, under the title: "Atypical Tuberculide Resembling Erythema Multiforme." As he saw only one case, he could not connect it with primary tuberculosis.

In Darier's "Précis de Dermatologie", I found one interesting sentence: "Si l'on se trouve en présence d'un de ces cas, que les travaux du Prof. Landouzy et de ces élèves ont montrés d'être assez fréquents, où l'érythème polymorphe se développe à la faveur de la tuberculose, il y a lieu de prescrire aux convalescents une hygiène appropriée et de les soumettre à une surveillance prolongée."

As in those days erythema nodosum was included with erythema multiforme, I cannot make out to what symptoms Landouzy referred. In the French bibliography after the war, I also found a few cases. In the Swedish bibliography I saw the report of a case that ended fatally and post-mortem examination was performed. A primary focus in the lung was found (the case was published for a different reason).

Assuming that an idiopathic form of erythema multiforme Hebræ actually exists, I suggest that where a disease of known ætiology but resembling the skin eruption of that disease is described, it should be named in such a manner as to make evident the more marked characteristics.

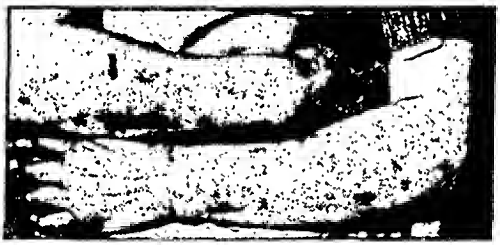


FIG 1.—Woman aged 60. Erythematous initial tuberculide.

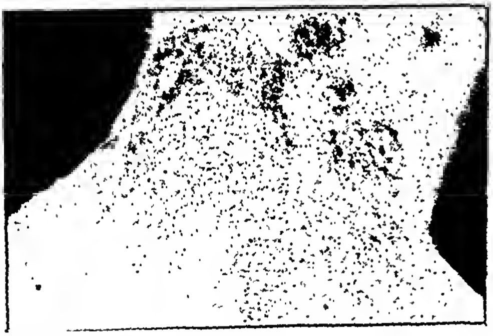


FIG. 2.—Woman aged 30. Erythematous initial tuberculide.

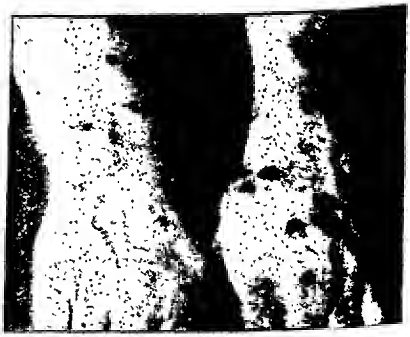


FIG. 3.—Woman aged 30. Erythematous initial tuberculide.

This dermatosis has some or all of the following characteristics:

(1) Rose-coloured to more livid patches, only slightly raised above the surface of the skin, with very little superficial infiltration; showing so little inflammatory œdema that the natural lines of the skin remain intact or are even more exaggerated; capricious of contour with a gradual change to the normal aspect of the skin and disappearing completely with diascopy; healing in a few days' to a few weeks' time whereby the efflorescence gets uniformly paler, and leaves no scars or pigmentation (*see* fig. 1).

[1] Bloch, B., *Schweiz. med. Wschr.* (1923) 53, 639.

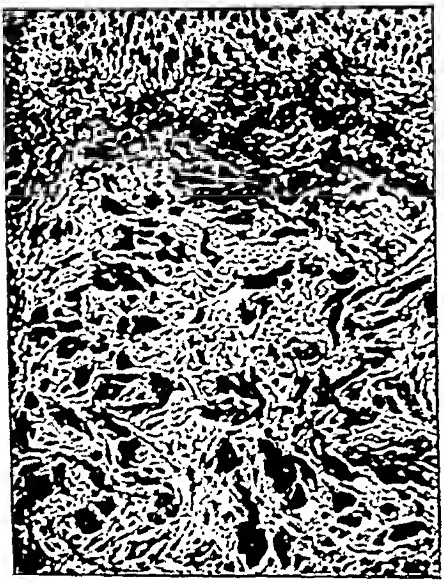


FIG. 3.—Forehead. Collagen bundles broken up and displaced by strands, fibrinoid and granular masses, stained yellow with van Gieson. Narrow subepidermal strip in this and the previous picture almost unchanged. × 170.

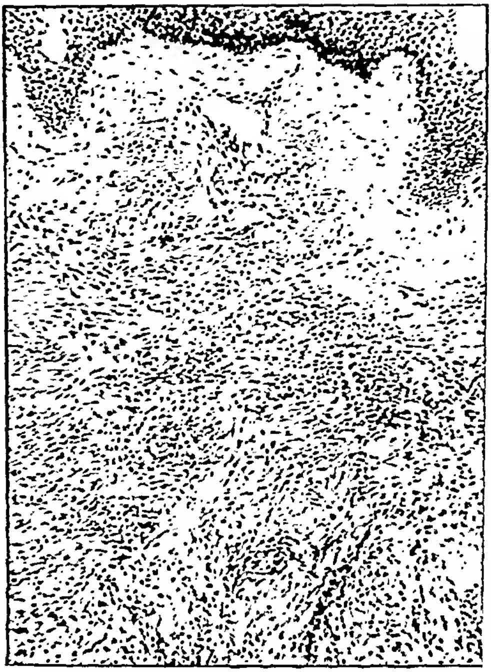


FIG. 4.—Forehead. Fairly dense cellular infiltrate, arranged diffusely or in short strands. A small amount of mucin in the right lower corner. × 80.

Dr. Brian Russell; The facial lesion seemed to me almost cartilaginous in texture, not œdematous. In the lesions on the arms there were a large number of discrete, dome-shaped papules, at the upper limit of the confluent infiltrated plaques.

It is interesting to note the lack of response to thyroid therapy. Pillsbury and Stokes (*Arch. Derm. Syph., Chicago* (1931) 24, 255) in their report on a case of the plaque type, state that this form arising in the pretibial region is always associated with exophthalmic goitre whereas the tuberose form, in which there is diffuse infiltration of the face, may, but often does not, react to thyroid treatment. This patient falls in the latter tuberose group.

Nodules in Abdominal Wall for Diagnosis ? Fibrosarcoma (Darier and Ferrand).—

A. C. ROXBURGH, M.D.

Mrs. M., aged 36. Complains of lumps in abdominal wall. Six years ago noticed painless lump in skin over left lower rib cartilages. Three to four years ago similar lumps right side of abdomen to right of operation scar. The lumps have increased in size and number. They are painless but irritate slightly. Patient is otherwise well. Periods regular, no pain, one child aged 7 years. No miscarriages.

Operations.—1923: Appendicitis and abscess. Tube in wound. Three months in hospital. 1924: Intestinal obstruction due to adhesions from previous operation. Scar right side, medial to other. 1937: "Twisted ovary" or "cyst of fallopian tube". Scar left side. Pleurisy March 1944, right base, with effusion. Similar attack December 1944 but no effusion. Subsequent X-rays show no abnormality in chest. Sputum, no tubercle bacilli December 1944.

Myxœdema Circumscriptum.—W. FREUDENTHAL, M.D.

Histological demonstration of Dr. Brian Russell's Case for Diagnosis, shown on October 17, 1946, *Proc. R. Soc. Med.*, **40,** 12 (*see* fig. 1).

For diagnostic purposes I excised a strip of tissue from the waxy plaque on the forehead and another from the border of the confluent area on the left arm including some outlying papules.

In both biopsies, particularly in the first, the cutis is considerably thickened and is extensively changed in its upper half, except for an almost normal narrow subepidermal strip. The collagen bundles are separated by an œdema, broken up and displaced by strands, fibrinoid and granular masses, stained yellow with van Gieson (figs. 2 and 3). In these areas there is a fairly dense infiltrate consisting of cells with pale or darkish oval nuclei which are arranged diffusely or in short, irregular strands (fig. 4).

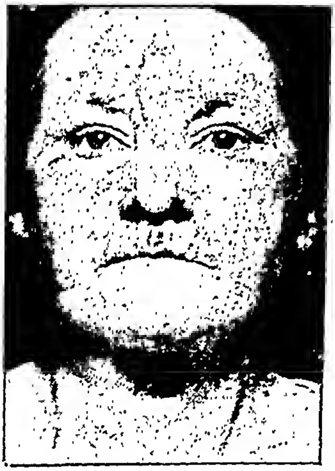


FIG. 1.—Myxœdema circumscriptum.

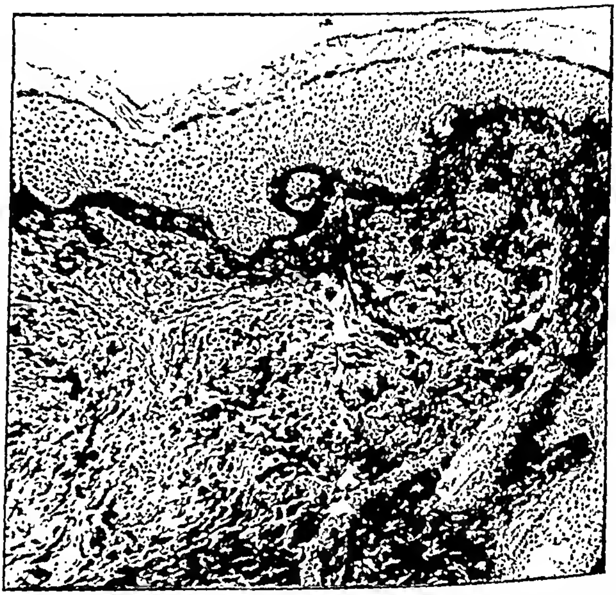


FIG. 2.—Arm. Across the border of the lesion. Connective tissue changes in the left half of the picture. van Gieson. × 70.

When stained with thionin or toluidin-blue large masses of mucin are seen, stained pink metachromatically. In the lesion from the arm mucin is found throughout the areas of altered connective tissue; in the lesion from the forehead it is mainly seen in the lower half of these areas whilst the upper half is free or shows only very little.

The presence of mucin confirms that this case belongs to the myxœdema group as I had suggested, on clinical grounds, when Dr. Russell demonstrated his case for diagnosis at the October meeting of this Section.

Clinically, the primary lesion is a dome-shaped papule which has a tendency to aggregate and later to coalesce, thus forming large sheet-like areas on the arms and hands. We are familiar with this development in other forms of circumscribed myxœdema, e.g. myxœdema moniliforme. In the waxy plaque on the face the papules can be seen only with difficulty, but they can still be felt. I have not seen a plaque like this in circumscribed myxœdema, but feel reminded of the facial changes occurring in generalized myxœdema.

Malling at my suggestion have been followed by some reduction in the redness and hardness of the lesions.

Dr. F. Parkes Weber: I should like to support a suggestion—actually made to me by Dr. Goldsmith—that these lesions are of the nature of keloid. But what is the nature of keloid? Ordinary keloid is, I suggest, a chronic *idiosyncratic* reaction towards some substance which is normally produced in connexion with the healing of wounds. The reason why most people do not develop keloid after wounds is, I suggest, that they lack the special idiosyncrasy. There may be, moreover, a factor in connexion with the healing of wounds which in some cases causes the production of a great deal more of this hypothetical substance than in other cases. I think we can go a stage further. What is probably very much rarer is the local production of this hypothetical keloid-causing substance, in connexion, not with wounds, but with various kinds of irritation, such, for example, as the constant rubbing of clothes about the waist. This suggestion would explain the extreme rarity of keloid without wounds of any kind. I suggest that the hypothetical keloid-causing substance is formed not only in connexion with actual wounds but occasionally (though extremely rarely) with other irritations of the skin. That is what I suggest has happened in the present case, and that would explain why the appearance of the main (active) lesions is that of a rosy coloured fairly active keloid. If I am correct, the probability is that ultimately, when the patient grows considerably older, the lesions will become paler, the rosy colour will be lost, and the keloid growth will shrivel. Is it worth while on this theory to try the effects of local X-ray therapy, such as, I know, occasionally produces the cure of ordinary keloids?

Dr. W. N. Goldsmith: It is true that I got the clinical impression of keloid before I knew anything of the histological structure; but there is, of course, the difficulty to which Dr. Parkes Weber has alluded, of the keloid arising where there is no scar. If, as Dr. Parkes Weber suggests, keloids are the result of an idiosyncratic reaction to a substance normally produced by healing wounds, one wonders why in this case there has been no such reaction in connexion with extensive scars elsewhere.

Dr. H. Corsi: The lesion does not appear to me in the least like a keloid: to say in words how we recognize physical signs, especially visual signs, is not easy; but in the main I would say that this lesion does not lie as near the surface as a keloid. A keloid is situated immediately under the epidermis, but this lesion lies deeper, a fact which is appreciable at the margins. There the edge of the tumour is palpable as it lies well below the normal skin. The tumour is, in fact, subcutaneous, but by extension towards the surface it has invaded and caused ulceration of the skin, and by extension deeply it has become attached to the costal cartilages.

I must disagree also with Dr. Parkes Weber's statement that spontaneous keloids, i.e. keloids not associated with any visible scar, are uncommon. I have seen a great number, particularly on the sternal region in women, a condition sometimes described as Alibert's disease.

Dr. Parkes Weber: I should like to point out that in my remarks I was referring only to the later lesions, those not connected with the operation.

Dr. A. C. Roxburgh: This condition does not look to me in the least like keloid. The lesions are not pink but brown, and not on the sites of the scars. On the left there is no scar near the lesion. This is some sort of fibrotic new growth, but not keloid.

Polymorphic Light Eruption.—F. Ray Bettley, M.D.

A. L., a male, aged 17. For fourteen years this patient has been subject to an eruption on the face, particularly in its upper part. The attacks occur only in summer, between the months of May and September and last some three or four weeks with incomplete remissions of about six weeks. Attacks do not appear to be related to particular exposures to sun, wind or other provoking cause. The eruption is itchy and consists of some vesicles, with scaly patches.

His general health has always been good; there is no family history of any skin disorder.

This year, for the first time, the eruption has lasted until the present time of year.

On examination.—There is a patchy scaly excoriated eruption symmetrically situated on the forehead, nose, and upper parts of the cheeks. No other abnormality found.

On examination: Brown, very hard, nodular masses in skin of abdominal wall over an area 5 by 2 in. to right of operation scars at outer side of right rectus abdominis mainly below level of the umbilicus. Similar but more massive area with depressed scaly centre in mid-clavicular line over the lower left costal cartilages, 2½ by 2½ in. This is seated upon and adherent to an underlying infiltrated area forming a somewhat raised cushion extending about ½ in. all round the surface lesion. Individual nodules are ¼ to ½ in. in diameter. The surface of the younger lesions is unaltered, that of the older ones is scaly or crusty (*see* fig.). They never break down or discharge and are unaffected by her menstrual periods. No viscus felt, no enlarged lymph glands.

Pathological examinations (November 1946).—W.R. and Kahn negative.

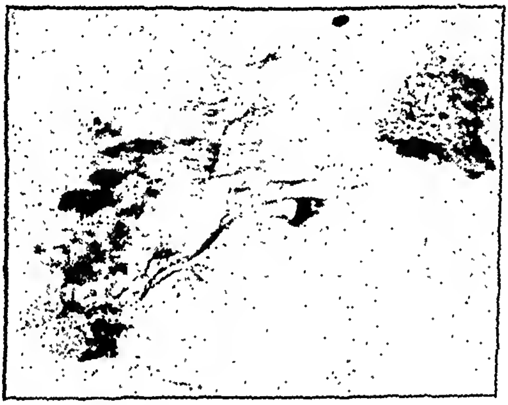


FIG. 1.—Dr. A. C. Roxburgh's case of fibrosarcoma of abdominal wall.

Biopsy (November 18, 1946).—From young nodule upper right abdomen (section shown).

Report (Dr. Muende).—The collagen in the mid-corium is very dense and numerous fibrocytes and groups of lymphoid cells can be found between the dense collagen bundles. The section shows no special pathological characteristics beyond these changes.

On December 6, 1946, the patient was put on a potassium iodide and mercury mixture t.d.s. as a therapeutic test and to-day shows some slight improvement. Probably another biopsy will have to be done from an older lesion.

Dr. Barber has suggested that the condition may be a type of the fibrosarcoma described by Darier and Ferrand (*Ann. Derm. Syph., Paris*, 1924, **5**, 545).

POSTSCRIPT (December 30, 1946).—A recent paper by O. G. Costa (*Arch. Derm. Syph., Chicago* (1946) **54**, 432) refers to one by G. W. Binkley (*Arch. Derm. Syph., Chicago* (1939) **40**, 578) which shows two photographs of lesions very like those in this case, one on the left side of the abdomen and one in the right supraclavicular fossa. Binkley draws attention to the tendency of dermatofibrosarcoma to occur on sites corresponding to the embryonic mammary ridge which would apply to both the lesions in this case. The sections reproduced in these papers seem to me to resemble that from this case.

POSTSCRIPT (March 14, 1947).—A further biopsy (10.1.47) taken from an old lesion in the centre of the mass on the right side of the abdomen was reported on by both Dr. Muende and Dr. Freudenthal as fibrosarcoma. A curious feature is that three intravenous injections of N.A.B. given by Dr. Vincent Bates of West

Malling at my suggestion have been followed by some reduction in the redness and hardness of the lesions.

Dr. F. Parkes Weber: I should like to support a suggestion—actually made to me by Dr. Goldsmith—that these lesions are of the nature of keloid. But what is the nature of keloid? Ordinary keloid is, I suggest, a chronic *idiosyncratic* reaction towards some substance which is normally produced in connexion with the healing of wounds. The reason why most people do not develop keloid after wounds is, I suggest, that they lack the special idiosyncrasy. There may be, moreover, a factor in connexion with the healing of wounds which in some cases causes the production of a great deal more of this hypothetical substance than in other cases. I think we can go a stage further. What is probably very much rarer is the local production of this hypothetical keloid-causing substance, in connexion, not with wounds, but with various kinds of irritation, such, for example, as the constant rubbing of clothes about the waist. This suggestion would explain the extreme rarity of keloid without wounds of any kind. I suggest that the hypothetical keloid-causing substance is formed not only in connexion with actual wounds but occasionally (though extremely rarely) with other irritations of the skin. That is what I suggest has happened in the present case, and that would explain why the appearance of the main (active) lesions is that of a rosy coloured fairly active keloid. If I am correct, the probability is that ultimately, when the patient grows considerably older, the lesions will become paler, the rosy colour will be lost, and the keloid growth will shrivel. Is it worth while on this theory to try the effects of local X-ray therapy, such as, I know, occasionally produces the cure of ordinary keloids?

Dr. W. N. Goldsmith: It is true that I got the clinical impression of keloid before I knew anything of the histological structure; but there is, of course, the difficulty to which Dr. Parkes Weber has alluded, of the keloid arising where there is no scar. If, as Dr. Parkes Weber suggests, keloids are the result of an idiosyncratic reaction to a substance normally produced by healing wounds, one wonders why in this case there has been no such reaction in connexion with extensive scars elsewhere.

Dr. H. Corsi: The lesion does not appear to me in the least like a keloid: to say in words how we recognize physical signs, especially visual signs, is not easy; but in the main I would say that this lesion does not lie as near the surface as a keloid. A keloid is situated immediately under the epidermis, but this lesion lies deeper, a fact which is appreciable at the margins. There the edge of the tumour is palpable as it lies well below the normal skin. The tumour is, in fact, subcutaneous, but by extension towards the surface it has invaded and caused ulceration of the skin, and by extension deeply it has become attached to the costal cartilages.

I must disagree also with Dr. Parkes Weber's statement that spontaneous keloids, i.e. keloids not associated with any visible scar, are uncommon. I have seen a great number, particularly on the sternal region in women, a condition sometimes described as Alibert's disease.

Dr. Parkes Weber: I should like to point out that in my remarks I was referring only to the later lesions, those not connected with the operation.

Dr. A. C. Roxburgh: This condition does not look to me in the least like keloid. The lesions are not pink but brown, and not on the sites of the scars. On the left there is no scar near the lesion. This is some sort of fibrotic new growth, but not keloid.

Polymorphic Light Eruption.—F. Ray Bettley, M.D.

A. L., a male, aged 17. For fourteen years this patient has been subject to an eruption on the face, particularly in its upper part. The attacks occur only in summer, between the months of May and September and last some three or four weeks with incomplete remissions of about six weeks. Attacks do not appear to be related to particular exposures to sun, wind or other provoking cause. The eruption is itchy and consists of some vesicles, with scaly patches.

His general health has always been good; there is no family history of any skin disorder.

This year, for the first time, the eruption has lasted until the present time of year.

On examination.—There is a patchy scaly excoriated eruption symmetrically situated on the forehead, nose, and upper parts of the cheeks. No other abnormality found.

Investigations.—Coproporphyrins are present in the urine to the extent of 4 mg. per litre in the specimen quantitatively examined. The estimated porphyrin excretion in this patient is forty times the normal.

Serum proteins normal.

Reaction to a test dose of ultraviolet (mercury vapour) normal.

Normal reactions were also obtained to infra-red, visible red, and artificial white (electric filament lamp) light.

Treatment and progress.—No improvement while in hospital in a shaded part of the ward. No improvement resulted from the application of 10% tannic acid in an emulsified base, nor from a lotion of 5% quinine bihydrochloride.

Hyperkeratosis Follicularis et Parafollicularis in Cutem Penetrans (*Kyrle*[1]).—J. R. SIMPSON, M.B.

Miss A. W., aged 63. Housekeeper.

History.—Seven years ago multiple horny pimples first appeared on the backs of her fingers, hands and forearms, and soon spread to her legs, ankles and feet. Apart from their unsightliness, the only symptom has been a mild sensation of pricking in each lesion when it reaches full development; in her own words, "when they prick me, I pull them out".

She has suffered from a mild otitis externa for some years. Her general health has been good except that she is subject to bronchitis and had brachial neuritis in 1943 and again earlier this year.

There is no family history of any skin disease.

On examination.—On the back of the hands and of the proximal phalanges and on the forearms, knees, legs, ankles and the dorsa of the feet, there are multiple discrete lesions varying from 0·5 mm. to 4 mm. in diameter. They are small brownish-yellow, horny papules with a rough surface. Some, but not all, are related to hair follicles. The horny plugs can easily be shelled out, leaving smooth round pits, the bases of which are red, but do not bleed.

There are a few yellowish-brown macules interspersed with the above, chiefly about the ankles, but the patient states that these appeared independently and not on the sites of previous horny pimples.

Histology (Material taken from the leg).—There is hyperkeratosis and a dense, wide horny mass has pushed down the deeper layers of the epidermis to the level of the junction of the reticular and papillary parts of the corium. In the deepest part there is parakeratosis and the underlying granular layer is absent.

There is acanthosis on either side of and beneath the horny mass, but in one place the basal layer is absent and the prickle-cell layer is thin and invaded by a dilated blood-vessel, from which there has been some extravasation of erythrocytes.

The corium shows no pilosebaceous structures, but around the lesion there is a moderately dense infiltration of lymphocytes and fibroblasts. The vessels are dilated and show endothelial proliferation.

Treatment.—Vitamin A, 100,000 i.u. daily, orally for three months.

Since I last saw her, a month ago, there has been a striking regression of the lesions, which are smaller and less numerous.

Dr. W. J. Hohmann: I have seen several cases of vitamin A deficiency in Holland. In most of them I made estimations of the vitamin A of the blood serum and found very low values. It seemed to me that this condition was part of a vitamin A deficiency. My cases improved after administration of vitamin A, but it takes some time before improvement can be seen. I think that Kyrle's disease is not a separate entity, but is a part of a vitamin A deficiency.

---

[1] *Arch. Derm. Syph.* (1916) 123, 466.

Section of Anæsthetics

President—STANLEY ROWBOTHAM, M.D.

[*January* 3, 1947]

DISCUSSION: ANÆSTHESIA FOR ABDOMINO-PERINEAL OPERATIONS FOR CANCER OF THE RECTUM

Dr. Ronald Jarman: Exactly forty years ago W. Ernest Miles performed his first operation for cancer of the rectum, and it is this operation which bears his name. The first three operations for this condition did extremely well, but subsequent results varied. Experience, improvement of technique and team work have now reduced the mortality rate to less than 5%, which my experience of over 1,000 cases has proved. From 1907 to the present date the general technique has improved and with it the anæsthesia as the list shows. Spinal analgesia has replaced ether and chloroform, thus getting the maximum relaxation without the use of irritant vapours, nitrous oxide and oxygen being used to keep the patient asleep. The premedication has become more or less standardized, omnopon 1/3 grain and scopolamine 1/150 grain are given to the average adult one hour before the operation; this produces a somnolent state and facilitates the giving of nitrous oxide and oxygen.

The introduction of intravenous anæsthesia fifteen years ago has abolished all psychic shock, the patient being put to sleep in bed and conscious only of a slight prick in the arm and oblivious of all further manipulations. This form of anæsthesia is either maintained by nitrous oxide and oxygen or by the administration of more of the intravenous drug.

ANÆSTHESIA FOR ABDOMINO-PERINEAL EXCISION IN CANCER OF THE RECTUM.

January 7, 1907.

W. Ernest Miles did his first abdomino-perineal operation for cancer of the rectum, the anæsthetic being ether, using a Clover's inhaler.

	Premedication	Anæsthetic
1908	Atropine	Open ether
1910	,,	Chloroform and ether mixture, followed by chloroform
1912	Atropine and scopolamine	,, ,, ,, ,, ,, ,, ,,
1917	,, ,,	Open ether
1919	,, ,,	Stovaine. Spinal
1920	,, ,,	Gas and oxygen. Stovaine
1924	,, ,,	,, ,, ,, ,, Sacral block novocain 20 c.c. 2%
1927	,, ,,	,, ,, ,, ,, ,, ,, ,, 40 c.c. 1%
1929	,, ,,	Spinocaine. Gas and oxygen (Jarman)
1930	Omnopon and scopolamine	Gas and oxygen. Nupercaine 18 c.c. 1 in 1,000
1931	,, ,,	,, ,, ,, ,, ,, ,, 1 in 1,500
1932	,, ,,	Nembutal 3·5 c.c. Gas and oxygen. Nupercaine 1 in 1,500
1932	,, ,,	,, ,, ,, ,, ,, ,, ,, 12 c.c. 1 in 1,500
1932	,, ,,	,, ,, ,, ,, ,, ,, ,, 1·5 c.c. 1 in 200
1933	,, ,,	Evipan 10 c.c. 10% solution. Gas and oxygen. Nupercaine 14 c.c. 1 in 1,500
1935	,, ,,	Pentothal 7 c.c. 10% solution. ,, ,, ,, Nupercaine 14 c.c. 1 in 1,500
1935	,, ,,	Pentothal 10 c.c. 5% solution. ,, ,, ,, Nupercaine 15 c.c. 1 in 1,500
1946	Omnopon 1/3 gr. and scopolamine 1/150 gr.	Pentothal 10-20 c.c. 5% solution. Gas and oxygen. Nupercaine 12-15 c.c. 1 in 1,500 and ephedrine 1 gr.

As a result of these advances chest and abdominal complications are fewer.

The age-incidence of cancer of the rectum varies from 17 years to 82 years, the average being between 60 and 75 years.

Blood-pressure.—The routine charting of blood-pressures as well as respirations, pulse-rate and the various anæsthetic agents used, has assisted the anæsthetist to keep a watchful eye on the patient's condition. The giving of an injection of ephedrine 1 grain immediately before the spinal, following the work of Sebrecht of Bruges and his assistants, has prevented anxiety in the early stages of the operation. Dr. Frankis Evans' method of giving an adrenaline drip during the operation has definitely increased the safety margin. As long as the pulse-rate does not rise unduly, I do not use cardiac stimulants, no matter how low the blood-pressure falls. This fall is very marked when the patient is turned on to his side for the perineal part of the operation and sometimes cannot be recorded. If the pulse-rate starts to rise with this fall in blood-pressure, an intravenous drip is established immediately, and, if necessary, whilst this is being done, 2 or 3 c.c. of anacardone are given intramuscularly.

It is all important that the patient is well oxygenated during the operation and that special attention is paid to raising the percentage of the oxygen at this stage.

If a large number of anæsthetic charts of this particular operation are examined, it is noticed that if the pulse-pressure is low then the blood-pressure falls rapidly but if the pulse-pressure is medium or high, the fall is slow and very rarely calls for anxiety. Warmth and blood transfusions soon restore the blood-pressure to within reasonable limits.

Blood transfusions.—These are given immediately after the operation, followed by water and glucose 5% in sterile vacolitres. This measure is only adopted during the operation if the patient's condition demands it. There is no doubt that this part of the technique has gone a long way to make the operation safer.

Position of the operating table.—The new operating tables can be put into a Trendelenburg position of 60 degrees. This enables the surgeon to get the growth away and establish a new pelvic floor, making the perineal part of the operation quite a short procedure.

Routine treatment.—The patient should be admitted to hospital or nursing home for at least fourteen days prior to the operation. During this time the physician, surgeon, pathologist, dental surgeon and anæsthetist are able to examine the patient at their leisure and have a meeting about the case. The upper respiratory tract, especially the teeth, should be thoroughly investigated.

High colonic wash-outs are given over a period of days. The patient has large doses of sulphasuxadine by mouth to sterilize the bowel. Since this has been done, peritonitis following the operation has been eliminated. This has been ably described by Mr. Alan Hunt (*Proc. R. Soc. Med.*, 1946, **39**, 549).

The *physiotherapist* teaches the patient how to use all his muscles whilst lying in bed, especially how to breathe and use his abdominal muscles. It is during this period that the anæsthetist visits the patient so as to get to know him and at the same time to create confidence. It is most important to make the patient realize that he is the centre of the picture and that everything is being done for his comfort and safety.

Sigmoidoscopy.—The most important examination is that of a sigmoidoscopy and biopsy. Not only does it establish the diagnosis but it helps the anæsthetist to see how the patient reacts to the anæsthetic and the various drugs that he is given as well.

The day of the operation.—The patient has had a good night, assisted by medinal

10 grains and aspirin 10 grains. One hour before the operation he is given his injection of omnopon 1/3 grain and scopolamine 1/150 grain, followed by a small dose of 5% solution of pentothal just before he is moved to the theatre, where he has a spinal of light nupercaine 1 in 1,500 given, preceded by an injection of ephedrine, then surgical sleep is established by nitrous oxide and oxygen, assisted by a further injection of pentothal if required. The anæsthetist helps in getting the patient ready by emptying his bladder, adjusting shoulder rests and making sure that the table is in the right position.

The technique has enabled the surgeon to complete the straightforward case in under an hour and has also helped him to make the inoperable case operable, ensuring that all cases are in moderate comfort during their final days.

Sterilization of syringes and needles.—It is of interest at this point to describe how all the syringes and needles are kept sterile. They are always cleaned out with triple distilled water and then put into pure industrial spirit for at least an hour before the operation. Prior to use, they are again washed and kept covered in triple distilled water. This is important for all injections, no matter what it is for. This method has been checked up by the pathologist a number of times and no bacteria have been found. It is accepted that the dry autoclave is the safest method in large institutions. Boiling and heat are only resorted to in cases of sepsis.

Other methods of anæsthesia.—Several of my series have been done under complete intravenous anæsthesia, assisted by nitrous oxide and oxygen, a few have had curare, but it is my firm belief at the moment that the method of choice is the one described, namely suitable premedication, pentothal, spinal anæsthesia maintained by nitrous oxide and oxygen.

After-care.—The after-treatment is very much in the hands of the skilled nurses, who are supervised by the surgeon:—The control of the blood drip followed by water and 5% glucose for several days; the watching of the colostomy, moving of the patient, drugs, feeding and making sure that the stomach does not become dilated. To keep muscle tone and to avoid chest symptoms the patient is encouraged to get out of bed the next day or the day after. Breathing exercises are re-established as soon as possible. All these various points are watched and it is fortunate that only a very few patients have sequelæ following the operation.

Paralysis, fatalities, &c.—Except in the early days when a sixth nerve palsy was observed and temporary trouble with the bladder, no trouble has been experienced due to nerve palsies. I have had five immediate fatalities on the operating table, subsequent post-mortems have shown three with coronary thrombosis and two with a fatty myocardium. The anæsthesia was in no way to blame for any of these disasters.

Resuscitation methods have had to be resorted to on several occasions, all successfully, except in the five cases just described. Collapse was attributed either to small pulse-pressure or to the patient being kept too long in a steep-Trendelenburg position. The most important cause, however, was the patient's own chronic nervous state and collapse would have occurred no matter what operation was performed. Various attempts have been made to correct these untoward happenings.

The physician has been asked to have the chest X-rayed with special reference to the heart, a blood drip has been established, the position adjusted as far as possible and suitable medicaments given for all cases which gave us the slightest cause for anxiety. The greatest attention has been paid to the smallest detail to make sure that this operation would be successful. A great deal of this success is due to Mr. A. Lawrence Abel, who in turn was Mr. Ernest Miles' assistant and has now been responsible for the surgery of the majority of my series. His interest in the anæsthetic as well as the operation has inspired everybody to work for the patient.

Dr. Frankis Evans: Besides the abdomino-perineal excision, there are two other operations performed nowadays, the perineo-abdominal and the synchronous combined excision. In this latter operation two surgeons work simultaneously, one at the perineum and the other at the abdomen. It is claimed by the protagonists of this operation that it is possible by this method to remove growths which would otherwise be considered inoperable. Indeed, the operability figures with this operation are given as 84%.

In skilled hands the perineo-abdominal operation takes no longer than the synchronous combined method. I have seen Gabriel remove a rectum by his perineo-abdominal route in fifty to fifty-five minutes, and this is the time usually taken in the synchronous combined method.

It has been said that there is more shock associated with the synchronous operation than with the other, but I should not like to be definite on this, for I believe that the shock is largely proportional to the blood loss, and if hæmostasis is quick and accurate the loss of blood is appreciably diminished.

In the light of experience the anæsthesia for these operations has become very largely standardized. My own preference is for a spinal analgesic in combination with a dilute pentothal drip to maintain unconsciousness. This method has the advantage of blocking the upward sensory path thereby diminishing the nerve shock: it also tends to lower the blood-pressure. This is an advantage in that there is less bleeding from the perineal end, and, provided the fall of blood-pressure is not too profound, is of distinct benefit to all concerned.

The choice of spinal analgesia, whether it be a light or heavy solution, is really immaterial for it is only a question of personal preference. My own experience favours the heavy solution and I use quite a small dose in practice. I do not aim for a high spinal block and do not expect to obtain analgesia beyond the costal margin. The patient would resent exploration of the liver surface if it were not for the pentothal drip. The idea of this is to attempt to limit the blood-pressure fall as far as possible.

The technique of administration is quite simple. The patient is turned over on to the left side and the spinal tap is made in the third lumbar interspace. 1·2 c.c. of heavy nupercaine or "Spinal D" is taken up into the syringe and is expanded to 1·5 c.c. with cerebrospinal fluid. This volume is reinjected into the spinal canal. The patient is then turned over into the dorsal decubitus and placed in a 5 degrees Trendelenburg position immediately after he has been turned on to his back. The knees are flexed but the heels remain touching the stretcher. This gives the analgesia to costal margin. The intravenous drip is now set up, preferably into a vein on the right forearm. As a matter of fact I have designed, and use, a special needle cannula for this purpose. I do feel that a cannula is of the utmost importance and is very much preferred to a needle. Needles are apt to perforate veins while in situ, whereas cannulæ do not.

The intravenous drip we use at St. Mark's is that which was devised by Mr. Officer when he was R.S.O. at St. Mark's. It consists of a central mixing chamber into which two drips are fused, so that one can administer blood on the one side together with saline on the other, or if a simultaneous drip is not required it gives a quick change from one bottle of saline to the next without any cessation of drip.

If the cannula be placed in a vein in the right forearm the arm may be kept at the side of the patient, or if preferred it can be held on a board at right angles. This is not in the way of the assistant, but would interfere with the surgeon's work if it were placed in the left forearm on a board.

A blood-pressure cuff is placed upon the left arm, so that blood-pressure readings can be taken during the operation. For this purpose we use a Mendelssohn-Evans visual blood-pressure recording instrument, which works very well. As soon as the cannula is in the vein 0·4% pentothal in normal saline is run in at some 120 drops to the minute until the patient has fallen asleep. The rate of drip is then slowed to 50 or so drops to the minute, and the patient is kept in upper first plane anæsthesia, that is to say with a brisk lid reflex. As soon as the abdomen has been opened the pentothal drip rate is increased to 120 or so drops per minute again, to deepen the anæsthesia, so that the patient does not resent the examination of the liver. As soon as this has been accomplished the drip is again slowed and the patient brought back to the very light plane he was in before.

If the blood-pressure falls below 80 one can start an adrenaline drip on the other side of the Officer's apparatus. This runs concurrently with the pentothal drip. The adrenaline drip consists of 1/250,000 adrenaline and is made by adding 2 c.c. of 1/1,000 adrenaline to 500 c.c. of saline. Sometimes adrenaline oxidizes in ordinary normal saline but this can be prevented by the addition of 100 mg. of ascorbic acid from a sterile ampoule, or by bubbling carbon dioxide through the saline before adding the adrenaline. If desired the adrenaline may be added to the blood but in this case 100 mg. of ascorbic acid must be added to every 500 c.c. of blood before adding the adrenaline, otherwise the adrenaline is oxidized by the blood. If it is decided to administer adrenaline, the drip rate is adjusted to maintain the blood-pressure round about 100 to 110 mm. of mercury. There is no point in raising the blood-pressure beyond this otherwise the patient would lose blood unnecessarily. The adrenaline has certain beneficent effects: it raises the blood-pressure, thereby keeping the kidneys excreting, and dilates the coronary arteries, thereby improving the cardiac circulation. Admittedly there are theoretical risks of over-dosage which would result in ventricular fibrillation, but this only occurs with gross overdosage, and the fibrillation ceases within a minute of the drip being stopped. With reasonable care there is no likelihood of this happening and the adrenaline drip is continued post-operatively for some hours until the patient's own blood-pressure control has again come into action.

The adrenaline drip is continued post-operatively until the patient's own blood pressure control is re-established. This occurs from four to twelve hours after operation. In one of my cases the adrenaline drip was continued at intervals for two or three days post-operatively, after the patient had had considerable hæmorrhage owing to a surgical catastrophe, and it was found that her blood-pressure fell almost to nothing each time the drip was stopped. This patient made an uninterrupted recovery, and we now have quite a series of patients who undoubtedly owe their lives to this method of blood-pressure control. I do not suggest that it is necessary in every case or should be used as a routine, but where the blood-pressure falls unduly low there is the indication for adrenaline as the easiest means of keeping the blood-pressure at the level desired. Adrenaline is so rapidly oxidized in the body that the delicacy of control and the rapidity of response is one of the great advantages of the method.

As a result of this we have found that we now can tackle patients whom we would formerly have refused as being unsuitable for operation.

I have found the ordinary pressor drugs disappointing. The effects of ephedrine, methedrine and phedracin were too transient.

I have studied the figures at St. Mark's from 1939 onwards, and find that there is nothing to choose between the perineo-abdominal and the synchronous excision as regards mortality rate, which is fairly steady round 8% and 9%.

Pulmonary complications post-operatively do sometimes occur. In 60 excisions there were 8 chests, 4 of whom had bronchitis, 1 pleurisy, and 3 pneumonia. 20 patients had a spinal with gas-oxygen ether, and of these 4 had chest complications, that is 20%. Of 40 patients who had a spinal and dilute pentothal drip 4 developed chests (3 bronchitis and 1 pneumonia).

All our excision cases are given blood during the operation, and it is started after, or towards the end of, the perineal dissection. Cuthbert Dukes found by direct observation that the blood loss during these operations varies between 250 c.c. and 750 c.c. We give each patient a pint of blood, and continue with saline afterwards for thirty-six or forty-eight hours.

We have tried a few cases with curare instead of spinal, but the hæmorrhage from the perineal end was such as to hamper the surgeon, and the patients were apparently more shocked than if a spinal had been used.

In conclusion, I would like to stress the magnitude of the operation, whatever method of excision be used, and I feel that the time factor has to be considered from the point of view of hæmorrhage and resultant shock. Even so the death from carcinoma of the rectum with its ceaseless tenesmus and tormina is so distressing that we should be prepared to operate upon the so-called inoperable patients. It gives them the chance of a few months or even years of carefree life, free from pain and suffering. For these reasons I feel that we should never refuse to anæsthetize a patient upon the grounds that he is not fit to withstand the shock of the operation, or that he is too old.

Mr. O. V. Lloyd-Davies: Coupled with measures to keep the patient asleep spinal anæsthesia is, at present, the most suitable anæsthetic for combined excisions of the rectum.

In an operation of this magnitude there are, however, certain precautions to be taken and one of the most important of these is an adequate control of the blood-pressure. The turning of the patient during the operation lowers the blood-pressure very considerably and on occasion to a dangerous level.

The abdomino-perineal and perineo-abdominal methods require one or two turns respectively, but this turning factor can be completely overcome by using the lithotomy-Trendelenburg position (*Lancet*, 1939 (ii), 74). With the patient in this position the surgeon can perform either of the above methods and with two surgeons a synchronous combined excision can be performed. The intravenous adrenaline drip method of blood-pressure control has been a life-saving measure on several occasions.

The patient's response to adrenaline is usually very dramatic and care must therefore be taken to balance the rate of the drip accurately with the blood-pressure recordings. Gross fluctuations of the pressure may be serious for the patient and a rapid drip rate by which the patient is given more than half a litre of fluid in four hours may again be harmful. A falling pressure requiring an increase in the rate of drip to above this danger point should be dealt with by increasing the concentration of adrenaline solution.

If adrenaline has been used during the operation it must be continued in the ward until the normal vasomotor control mechanism recovers. This requires the constant attention of a person competent to take repeated blood-pressure recordings and to adjust the drip rate accordingly. In ideal circumstances there should be a post-operative team comparable with an operative team.

A poor-risk subject of 70 years with a massive growth made an excellent recovery after a combined excision and during the first three post-operative days he required 64 c.c. of adrenaline. At times the concentration of adrenaline was as much as 10 c.c. per half-litre.

Another interesting case of anuria thirty-six hours after a combined excision was successfully dealt with by introducing adrenaline into the drip, thereby raising her blood-pressure which was 70 mm. of mercury to her normal of 120 mm. of mercury. This case failed to respond to the usual measures.

Dr. V. Eades Vessell, having stated that the disadvantages and dangers resulting from the employment of adrenaline had been amply demonstrated by previous speakers, put in a strong plea for early blood drip transfusion during the course of the operation well before the onset of any evidence of shock. No risk was thereby incurred and, when this was done, in his opinion the post-operative work of the nursing staff was considerably lightened and the suffering and discomfort of the patient were diminished.

Dr. H. W. Loftus Dale had, for some years, used cyclopropane in conjunction with spinal analgesia for abdomino-perineal excisions of the rectum, believing that the increased oxygen used in conjunction with this agent made it preferable to nitrous oxide. Recently he had abandoned spinals in favour of curare thereby avoiding the fall in blood-pressure which accompanies movement of a patient from the Trendelenburg to the lateral position under a spinal. There was increased bleeding associated with the combination of cyclopropane and curare and he pointed out the danger of inadequate pulmonary ventilation in a patient with paresis of the diaphragm in the full Trendelenburg tilt.

Dr. Victor Goldman asked Dr. Frankis Evans if he had used methedrine instead of adrenaline as a drip infusion. Dr. Goldman was rather diffident about using adrenaline during general anæsthesia as it was his practice to maintain light anæsthesia with cyclopropane rather than nitrous oxide and oxygen. It was also his practice to add 30 mg. of methedrine to the pint of saline. Dr. Goldman also mentioned that he had anæsthetized a number of cases of perineo-abdominal resections by means of light cyclopropane anæsthesia using curare to produce muscular relaxation. There had been no complaints from the surgeons concerning the anæsthesia or increased bleeding.

The President (Dr. Stanley Rowbotham) said that his own experience of the abdomino-perineal operation extended well over twenty years, and although he had not anæsthetized as many cases as either Dr. Jarman or Dr. Frankis Evans, he had nevertheless had a fair experience of the operation, and with several surgeons. He agreed that spinal anæsthesia combined with a sleeping general anæsthetic appeared to give the best results. He was prepared to believe that curare might prove equally good, but so far he had had small experience of it in this particular field. From the small number of combined operations which he had anæsthetized he was inclined to think that patients became more shocked; perhaps because the trauma was concentrated over a shorter period of time.

He agreed with Dr. Frankis Evans that he preferred to have control of the circulation from the start, and not to wait for resuscitation until the patient had returned to bed. This meant putting up a drip before the operation started. He had used the adrenaline drip advocated by Dr. Frankis Evans many times. The idea originated from Crile; but adrenaline was only half the story; in the body adrenaline was rapidly destroyed by the ferment amylase oxidase. This ferment, however, could be fixed by ephedrine, so that if ephedrine were added to the adrenaline solution the action of the adrenaline was very considerably prolonged. He had been in the habit of using 1 c.c. of 1/1,000 solution of adrenaline and 5 grains of ephedrine hydrochloride in a half-litre bottle of saline. He had, however, given up the use of adrenaline since plasma or serum had become available, because these, having a big molecule, remained in the circulation and sustained the blood-pressure for a much longer period than did any other intravenous injection which he knew. In his opinion this was also superior to the many analeptic drugs which were available.

Dr. Frankis Evans, in reply to Dr. Goldman, said that he had not used methedrine as an infusion, but had only given it in intermittent dosage, 15 mgm. intramuscularly and 15 mgm. intravenously. He had used a combination of 1 in 250,000 adrenaline with ephedrine (gr. iii to 500 c.c.) with very satisfactory results.

Clinical Section

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[*December* 13, 1946]

Paterson-Plummer-Vinson Syndrome in a Case of Familial Acholuric Jaundice.—LEO RAU, M.D., M.R.C.P.

Miss E. S., aged 29, first seen in August 1946, complaining of dysphagia, first noticed in 1939. It occurred at irregular intervals of weeks or months, but was never severe enough to make her vomit. In 1945, she was seen by a surgeon who performed a partial thyroidectomy, but the attacks continued. They could not be connected with her periods, which were normal.

Family history.—One of her sisters has acholuric jaundice (*Proc. R. Soc. Med.*, 1946, **39**, 307), and in 1942 her mother was treated for pernicious anæmia for a period of less than three months, obviously a case of macrocytic anæmia.

20.8.46: Poor physical state, marked pallor, weight 8 st. 2 lb. No jaundice, cyanosis or œdema. B.P. 130/85. No glands palpable. No ulcers of the leg and no abnormality of the skin. There were some fissures of the lips. Spleen and liver could not be felt; there was marked atrophic glossitis; her nails were spoon-shaped, short and atrophic. With the exception of urobilinogen, no abnormality of the urine could be detected.

28.8.46: Seen after attacks of biliousness, giddiness and headaches. The serum bilirubin was 0·17 mg.% (indirect). Fragility of R.B.C. from 0·36% to 0·60% NaCl. The Price-Jones curve showed a shift to the left.

Radiological examination.—The barium swallow showed marked spasm of the œsophagus, just above the aortic knuckle, which would pass off and then allow some of the barium to reach the cardia. On reaching this area, retroperistalsis would start, until the barium had again returned to the spastic area. This interchange of spasm, peristalsis and retroperistalsis could be observed for long periods, until the œsophagus was found empty of barium. No abnormality of heart, chest, diaphragm, stomach, duodenum, or small intestine.

23.10.46: Spasm very marked, œsophagus still filled with barium after forty minutes (*see* table for blood-counts).

BLOOD-COUNTS.

Dates	20.8.46	28.8.46	4.9.46	2.10.46	23.10.46	27.11.46
R.B.C. (millions)	4·24	4·38	4·32	4·64	5·15	4·68
Hb%	60	47	60	92	108	96
W.B.C.	20,000	8,000	8,400	9,800	10,200	6,200
Differential:						
Poly. Neutros	74%	63%	53%	53%	73%	66%
,, Eosinos	1%	—	2%	1%	—	1%
,, Basos.	—	3%	2%	2%	2%	1%
Lymphocytes	24%	32%	40%	39%	24%	31%
Monocytes	1%	2%	3%	5%	1%	1%
Myelocytes (in addition)	4%	2%	3%	—	—	—
Anisocytosis	+	+	+	+	—	—
Poikilocytosis	+	+	+	+	+	+
Hypochromasia	—	—	+	+	—	—
Megalocytosis	—	—	—	+	—	—
Reticulocytes	3%	—	—	—	—	2%
ŒSOPHAGEAL SPASM as seen in X-ray	+	+	+	+	+	+

The President (Dr. Stanley Rowbotham) said that his own experience of the abdomino-perineal operation extended well over twenty years, and although he had not anæsthetized as many cases as either Dr. Jarman or Dr. Frankis Evans, he had nevertheless had a fair experience of the operation, and with several surgeons. He agreed that spinal anæsthesia combined with a sleeping general anæsthetic appeared to give the best results. He was prepared to believe that curare might prove equally good, but so far he had had small experience of it in this particular field. From the small number of combined operations which he had anæsthetized he was inclined to think that patients became more shocked; perhaps because the trauma was concentrated over a shorter period of time.

He agreed with Dr. Frankis Evans that he preferred to have control of the circulation from the start, and not to wait for resuscitation until the patient had returned to bed. This meant putting up a drip before the operation started. He had used the adrenaline drip advocated by Dr. Frankis Evans many times. The idea originated from Crile; but adrenaline was only half the story; in the body adrenaline was rapidly destroyed by the ferment amylase oxidase. This ferment, however, could be fixed by ephedrine, so that if ephedrine were added to the adrenaline solution the action of the adrenaline was very considerably prolonged. He had been in the habit of using 1 c.c. of 1/1,000 solution of adrenaline and 5 grains of ephedrine hydrochloride in a half-litre bottle of saline. He had, however, given up the use of adrenaline since plasma or serum had become available, because these, having a big molecule, remained in the circulation and sustained the blood-pressure for a much longer period than did any other intravenous injection which he knew. In his opinion this was also superior to the many analeptic drugs which were available.

Dr. Frankis Evans, in reply to Dr. Goldman, said that he had not used methedrine as an infusion, but had only given it in intermittent dosage, 15 mgm. intramuscularly and 15 mgm. intravenously. He had used a combination of 1 in 250,000 adrenaline with ephedrine (gr. iii to 500 c.c.) with very satisfactory results.

Treatment.—Excision head of radius and tendon transplantation. A 2-inch transverse dorsal wrist incision was made in a skin crease. Posterior annular ligament preserved, extensor tendons found to be thin and atrophic except for radial extensors. Extensor carpi radialis brevior detached from its insertion and sutured to extensor communis with fingers extended and communis tendon mass sutured together. Tendon of extensor carpi radialis longior split for about 2½ in. and one portion detached from its insertion threaded beneath posterior annular ligament with extensor pollicis longus, and sutured to that tendon with the thumb in extension.

After-treatment.—Cock-up splint for five weeks, fixing wrist and metacarpo-phalangeal joints. Interphalangeal joints moved from the first. There is now full flexion and extension of fingers and wrist and the elbow movements are normal. Scars are minimal, at dorsum of wrist and over head of radius. Patient is able to work as an artist and during the late war served throughout as an ambulance driver at home and overseas. (*See* photograph.)

Leontiasis Ossea.—J. M. WILLCOX, M.B. (for IVOR LEWIS, M.S., M.D.).

Elizabeth E., aged 55, housewife, admitted to hospital September 25, 1946.

History.—In 1929 X-ray showed what appeared to be an odontome of the left upper jaw. At operation three months later some bone was removed but the patient was told that the whole of the tumour was not removed for fear of breaking the jaw. Since 1930 her face has been slowly and steadily getting bigger. There has been no pain. The patient's only symptoms are the shape of her face and uselessness of the upper incisors.

On examination.—Bilateral enlargement of the maxillæ, making cheeks and upper jaw protrude. Subsidiary swellings both sides of nose. Alveoli enlarged and thickened. X-ray shows gross changes in both superior maxillæ with great bony thickening and a structureless sclerosis. Both antra are occluded. Middle and inferior turbinates similarly affected. Frontal bones show a few patches of sclerosis. X-ray appearances of pelvis and long bones normal. Wassermann reaction negative.

Dr. H. S. Stannus: Cases of leontiasis ossea present many points of interest; their ætiology remains unknown, their relationship to other conditions uncertain, including among them fibrocystic disease and the condition known as goundou commonly associated with yaws. Anyone interested in the subject should consult the monograph by Botreau-Roussel (1925) on "Ostéites pianiques." Some years ago I collected all the published cases of leontiasis and found I could match each one with a case from Botreau-Roussel's wonderful series. One wondered whether there was some common ætiological factor in the two conditions—possibly a nutritional factor disturbing bone metabolism. A rather similar affection occurs in caged anthropoids, equidæ and goats.

Malignant Synovioma of the Left Elbow.—RALPH SHACKMAN, F.R.C.S.

Mrs. O. S., aged 44, a housewife, was first seen in April 1940. She had rheumatoid arthritis which she said had been present for nineteen years. There were fusiform swellings of all the interphalangeal joints and all the metacarpo-phalangeal joints of the right hand. The right wrist, the right elbow and the right shoulder were all stiff. Crepitus was present in the right knee and there was ankylosis of the tarsal and metatarsal joints, a right hallux valgus and stiff inter-phalangeal joints of the right foot. The first and second digits of the left hand were swollen, the left wrist was slightly stiff: the left elbow and the left shoulder were stiff. There was crepitus of the left knee, a left hallux valgus and stiff inter-phalangeal joints of the left foot. The range of movement of the left elbow was from 35 to 160 degrees, and there was some limitation of pronation.

The koilonychia was still found on October 2, whereas the atrophic glossitis had disappeared when examined on that day.

A second fragility test (2.12.46) was again abnormal (0·32%—0·60% NaCl).

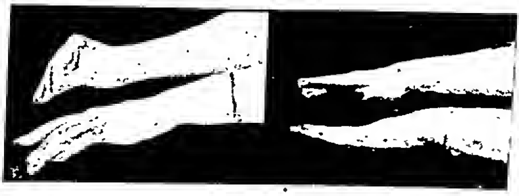
Treatment and progress.—Miss E. S. was put on Blaud's pills, b.d.ii, after the diagnosis was established on 4.9.46. There was an immediate response to this treatment.

Comment.—The leading symptom (dysphagia) in this patient is characteristic of microcytic anæmia, caused by iron deficiency. This Paterson-Plummer-Vinson syndrome, on radiological examination, could be localized to the upper third of the œsophagus, where there was marked spasm, just above the aortic knuckle. The sudden drop of hæmoglobin from 60% to 47% in the absence of any hæmorrhage suggested the probability of an acholuric jaundice, perhaps in addition to the microcytic anæmia. In favour of the presence of one of the hæmolytic anæmias —in this case acholuric jaundice—was the familial occurrence, the abnormal fragility of the R.B.C., the left shift of the Price-Jones curve, the raised reticulocyte count and the urobilinogenuria.

Dr. Herbert Levy said that this seemed to be a fortuitous combination of latent congenital hæmolytic anæmia (acholuric jaundice) and sideropenic dysphagia (Paterson-Plummer-Vinson's syndrome). In the series of cases of the latter condition reported by J. Waldenström and S. R. Kjellberg (*Acta radiol., Stockh.*, 1939, **20**, 618) and B. S. Holmgren (*Acta radiol., Stockh.*, 1943, **24**, 455) as well as in the case shown before this Section by Dr. K. P. Ball (*Proc. R. Soc. Med.*, 1945, **38**, 134) œsophageal narrowing was usually found just below the level of the cricoid cartilage whereas the present case was reported to show a transitory spasm as far down as the crossing of the aorta; strict adherence to the technique of the first-named authors might in the present case show an upper stricture besides the demonstrated abnormality. Patients suffering from sideropenic dysphagia were possibly prone to develop a retrolaryngeal or hypopharyngeal carcinoma and should be followed up for long periods with this complication in mind.

Tendon Transplantation for Posterior Interosseous Nerve Paralysis.—REGINALD A. KING, O.B.E., F.R.C.S.

Miss I. First seen on 25.5.38, aged 19. She complained of difficulty in using the right hand with inability to extend thumb and fingers at the metacarpophalangeal joints, since the age of 4, when she fell from a height of ten feet in S. Africa and fractured the right arm. The right hand was slightly smaller than the left; there was a slight prominence on the outer side of the forearm with wasting of the dorsal muscles. The head of the radius was dislocated outwards. Extensors indicis, digiti minimi, carpi ulnaris, digitorum communis and pollicis longus were paralysed. Extension of wrist was possible on the radial side as extensors carpi radialis longior, brevior and supinator longus contracted normally.


(*a*) (*b*)

Posterior interosseous nerve paralysis (*a*) before, (*b*) after tendon transplantation.

X-ray of forearm showed head of radius dislocated outwards and backwards with lengthening of radial neck.

X-rays of left elbow showed: "Joint spaces diminished with osteophytic lipping at the margins of the bones. Appearances suggest long-standing arthritis of the rheumatoid type." (This applied also to the X-ray appearances of all the clinically involved joints.)

The patient continued under supervision and made no special complaint about the left elbow until August 1946 (i.e. six and a quarter years after she was first seen) when she stated that in December 1945 she had noticed sudden pain and swelling in the left elbow. The pain and swelling persisted and were not relieved by poulticing. Now, the left elbow was swollen to the size of a grapefruit, with dilated veins in the over-lying skin. The range of movement was 90 to 135 degrees, and there was some limitation of pronation and supination. The axillary lymph nodes were not palpable. On questioning, the patient admitted to "pins-and-needles" being felt in the tips of the third, fourth and fifth fingers. The swelling was soft and felt as if it contained fluid, but aspiration failed to confirm this clinical impression. On September 27, 1946, a biopsy was carried out. A moderate amount of thickened fibrinous exudate was drained and a piece of soft tissue removed for histological examination. The wound healed by first intention.

Histological report (Dr. C. V. Harrison).—"Most of the tissue is well outside the joint in the voluntary muscle. The tissue is infiltrated by a densely cellular malignant tumour composed of irregularly rounded cells with pale-staining vacuolated nuclei and prominent nucleoli, and is devoid of any definite structural pattern. The cells appear to be of mesoblastic origin and show frequent mitoses. It is considered that this is a malignant mesoblastic tumour, probably a synovioma." Reticulum staining shows a rich network of reticulin fibrils. (*See* figs.)

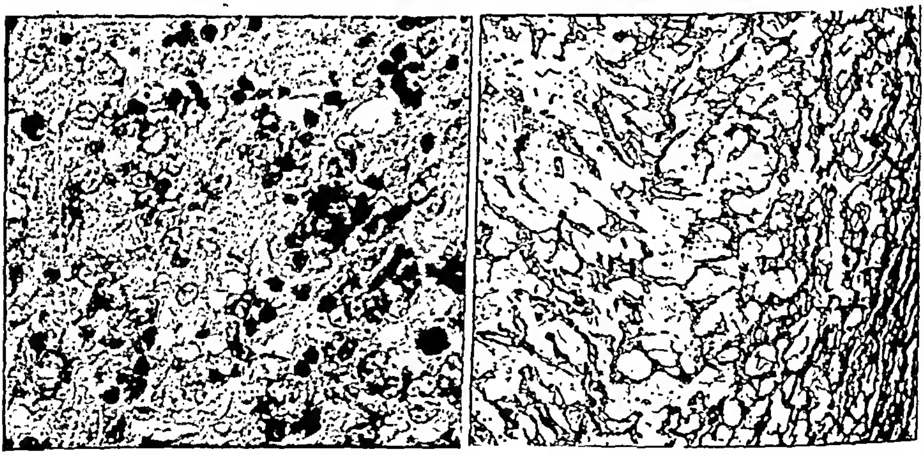


FIG. 1. ×394 FIG. 2. ×116

Malignant Synovioma of Left Elbow.

Fig. 1.—Hæmatoxylin and eosin staining. Fig. 2.—Silver impregnation, reticulum staining.

X-ray of the chest showed no metastases and a disarticulation at the left shoulder joint was performed under general anæsthesia.

Primary healing followed and convalescence was smooth. Deep X-ray therapy has been given to the shoulder. The elbow was dissected and pieces of the fleshy white tumour were taken for histology: one from the synovium of the elbow-joint, one from around the ulnar nerve, and one enlarged axillary lymph gland noted at operation. All three showed a tumour similar to that of the biopsy, but with the histology less well preserved.

Diagnosis was suggested as a result of the biopsy, which showed tissue reproducing caricatures of synovial structures with marked reticulin formation, and sarcomatous cells. The tumour appears to be of that group enunciated by Louis Berger (*Amer. J. Cancer,* 1938, **34**, 501) as the "indifferent type, of compact structure but with clear spots after reticulum impregnation, corresponding to a beginning endothelial evolution". Confirmation was obtained after disarticulation by the dissection which showed the tumour to have arisen in the soft tissues around the left elbow-joint.

Prognosis is considered to be poor in view of the series reported by Haagensen and Stout (*Ann. Surg.*, 1944, **120**, 826) who collected 104 cases of whom only 3 were known to be free from recurrence or metastasis after five years.

Transthoracic Partial Gastrectomy for Intussuscepted Fibromyoma of Fundus of Stomach.—Norman C. Tanner, F.R.C.S.

S. C., a Polish journalist aged 56, was admitted to St. James' Hospital on 30.10.46, having collapsed after three days' melæna. He stated that there had been some abdominal discomfort after meals for a few months. Six weeks previously he had vomited blood. He had been losing weight.

On examination he was found to be very pale and thin. B.P. 100/46. No mass could be felt in the abdomen. Blood-count on day of admission: R.B.C. 1,940,000 per cmm., Hb 28%. He was given a blood transfusion and early light feeding and there was no further massive hæmorrhage.

Five days after admission a gastroscopic examination disclosed the presence of a polypus of the fundus of the stomach with the "bridging folds" sign of Schindler at the base and a white polypoidal edged ulcer at its apex (*see* Plate). The mucosa of the stomach was atrophic but no other tumour of the stomach was present. Fractional test meal revealed complete achlorhydria. Later he began to get pain after meals again, and an X-ray examination about this time showed a filling defect, evidently the stalk of a mass which originated at the fundus of the stomach. The tumour itself, thinly covered with barium, appeared to be intussuscepted into the duodenum. The gastroscope was passed again at this time but unobstructed views could not be obtained, which tended to confirm that some gross anatomical distortion had taken place.

Operation.—On 29.11.46, under cyclopropane and local anæsthesia, a transthoracic transphrenic laparotomy was performed, after removing the tenth rib. The fundus of the stomach was found to be intussuscepted, the apex of the intussusception being a hard tumour lying in the grossly distended duodenum. The intussusception was easily reduced. In view of the extremely hard consistency, nodularity of the base of the tumour, enlargement of the paracardial and superior gastric lymph glands, and the persisting ulceration, a radical resection was carried out, the upper two-thirds of stomach, 3 cm. of œsophagus, spleen and neighbouring omenta and glands being removed. After closing the cut end of the lower segment of the stomach an "end-in-side" œsophago-gastrostomy was performed. The remaining stomach was securely anchored and diaphragm and chest were closed with drainage of the pleural cavity.

The post-operative progress was normal, fluids by mouth were taken on the second day, he was up on the sixth day and was discharged, taking food very well, on 21.12.46.

The specimen.—The tumour, 12 cm. by 7 cm. by 7 cm. has its base about 2 cm. from the cardiac orifice. It is hard in consistency and has an ulcer crater at the

PROC. ROY. SOC. MED.
Vol. XL, No. 6.
Clinical Section

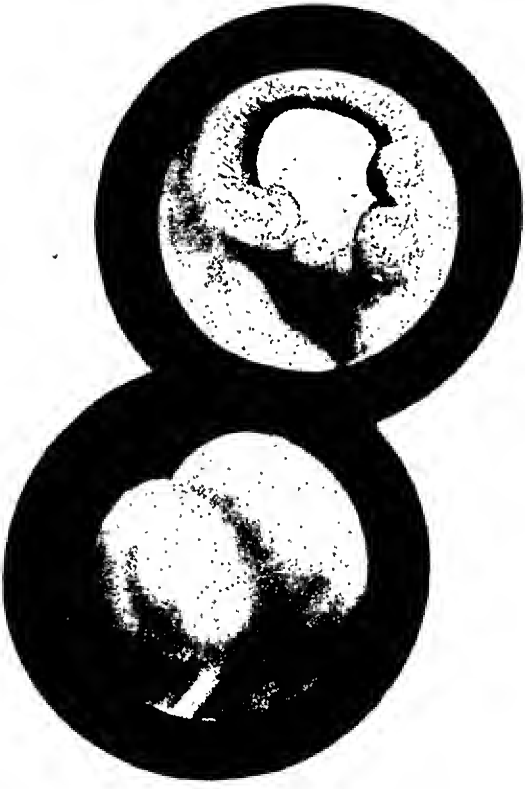

P. Startup.

FIG. 1.—Gastroscopic painting of two parts of ulcerating polypus.

NORMAN C. TANNER: Transthoracic Partial Gastrectomy for Intussuscepted Fibromyoma of Fundus of Stomach.

Diagnosis was suggested as a result of the biopsy, which showed tissue reproducing caricatures of synovial structures with marked reticulin formation, and sarcomatous cells. The tumour appears to be of that group enunciated by Louis Berger (*Amer. J. Cancer*, 1938, **34**, 501) as the "indifferent type, of compact structure but with clear spots after reticulum impregnation, corresponding to a beginning endothelial evolution". Confirmation was obtained after disarticulation by the dissection which showed the tumour to have arisen in the soft tissues around the left elbow-joint.

Prognosis is considered to be poor in view of the series reported by Haagensen and Stout (*Ann. Surg.*, 1944, **120**, 826) who collected 104 cases of whom only 3 were known to be free from recurrence or metastasis after five years.

Transthoracic Partial Gastrectomy for Intussuscepted Fibromyoma of Fundus of Stomach.—NORMAN C. TANNER, F.R.C.S.

S. C., a Polish journalist aged 56, was admitted to St. James' Hospital on 30.10.46, having collapsed after three days' melæna. He stated that there had been some abdominal discomfort after meals for a few months. Six weeks previously he had vomited blood. He had been losing weight.

On examination he was found to be very pale and thin. B.P. 100/46. No mass could be felt in the abdomen. Blood-count on day of admission: R.B.C. 1,940,000 per cmm., Hb 28%. He was given a blood transfusion and early light feeding and there was no further massive hæmorrhage.

Five days after admission a gastroscopic examination disclosed the presence of a polypus of the fundus of the stomach with the "bridging folds" sign of Schindler at the base and a white polypoidal edged ulcer at its apex (*see* Plate). The mucosa of the stomach was atrophic but no other tumour of the stomach was present. Fractional test meal revealed complete achlorhydria. Later he began to get pain after meals again, and an X-ray examination about this time showed a filling defect, evidently the stalk of a mass which originated at the fundus of the stomach. The tumour itself, thinly covered with barium, appeared to be intussuscepted into the duodenum. The gastroscope was passed again at this time but unobstructed views could not be obtained, which tended to confirm that some gross anatomical distortion had taken place.

Operation.—On 29.11.46, under cyclopropane and local anæsthesia, a transthoracic transphrenic laparotomy was performed, after removing the tenth rib. The fundus of the stomach was found to be intussuscepted, the apex of the intussusception being a hard tumour lying in the grossly distended duodenum. The intussusception was easily reduced. In view of the extremely hard consistency, nodularity of the base of the tumour, enlargement of the paracardial and superior gastric lymph glands, and the persisting ulceration, a radical resection was carried out, the upper two-thirds of stomach, 3 cm. of œsophagus, spleen and neighbouring omenta and glands being removed. After closing the cut end of the lower segment of the stomach an "end-in-side" œsophago-gastrostomy was performed. The remaining stomach was securely anchored and diaphragm and chest were closed with drainage of the pleural cavity.

The post-operative progress was normal, fluids by mouth were taken on the second day, he was up on the sixth day and was discharged, taking food very well, on 21.12.46.

The specimen.—The tumour, 12 cm. by 7 cm. by 7 cm. has its base about 2 cm. from the cardiac orifice. It is hard in consistency and has an ulcer crater at the apex. On inserting a probe the ulcer is found to penetrate right to the base of the tumour. Other smaller and more superficial ulcers lie on the tumour. At its base outside the stomach are several small prominences which on section were found to be a part of the main tumour. The cut surface of the tumour has an appearance similar to that of a uterine fibroid.

Histological report (Dr. Anne Gibson).—The main tumour is composed of unstriated muscle cells and fibroblasts. These cells are regular in size and staining and show no tendency to invade the atrophied layer of stomach mucosa which covers the tumour. The section of a subsidiary nodule at the base of the tumour shows similar appearances, but here many of the cells are vacuolated and the nuclei are therefore compressed. Appropriately stained sections show that this vacuolation is not due to the presence of fat. This portion of growth is surmounted by a compressed layer of fibrous tissue and there is no histological evidence of lymphoid tissue.

Comment.—Intussusception of a gastric polypus into the duodenum is a well-known complication, and it was no doubt the cause of the pain in this case. The transthoracic route undoubtedly gave the best possible approach to the tumour, and the radical resection performed would not have been possible by an abdominal route. The after-histories of leiomyomata (of which this fibromyoma must be considered a variety) show that a large number eventually become malignant. The short history of this case, the large size, persistent and multiple irregular ulceration of the tumour led to suspicion of its innocence. Histological examination shows no evidence of malignancy, although it is occasionally misleading. The deep ulceration may have persisted as a result of the prolapse into the duodenum, or it may be that it in part resulted from cystic degeneration of the tumour, a degeneration to which the gastric leiomyomata are prone.

Two Cases of Transthoracic Gastrectomy.—NORMAN C. TANNER, F.R.C.S.

I.—A. T., male, aged 42. Epigastric pain after meals for six months.

7.12.45: Admitted to St. James' Hospital with hæmatemesis. X-ray and gastroscopy revealed presence of indurated ulcer just below cardia. This failed to improve on a medical régime.

21.2.46: Operation by abdominal and left thoracic (9th intercostal space) approach. Malignant ulcer penetrating pancreas found. Radical total gastrectomy, splenectomy and two-thirds pancreatectomy performed. Union by end-to-end œsophago-jejunostomy after "Roux" mobilization of jejunum.

Histological report.—"Columnar-celled adenocarcinoma."

Progress.—Patient discharged well on 8.6.46. Is now working and has no signs of pancreatic deficiency.

II.—P. G., male, aged 45. One year increasing pallor, epigastric pain.

On examination.—Epigastric mass. 9.10.46: Gastroscopy—4 cm. below cardia ulcerated carcinoma of the stomach. 17.10.46: Operation: total gastrectomy by combined abdominal and thoracic approach with end-to-end œsophago-jejunostomy (Roux loop).

Pathological report.—Adenocarcinoma. (Specimen was shown.)

Section of Laryngology

President—NORMAN PATTERSON, F.R.C.S.

[*December* 6, 1946]

Emergency Epistaxis

By JOSEPHINE COLLIER

BLEEDING from the nose generally ceases spontaneously no matter what treatment is adopted, but when persistent it may lead to a serious degree of anæmia and occasionally it is a cause of death. In the Registrar-General's Reports epistaxis is classified under the heading of "other diseases of the circulatory system" so one cannot judge the frequency of its occurrence as an immediate cause of death but most of us must have known or heard of cases where death has followed bleeding from the nose in such a manner that whatever circulatory disease was present one must honestly say that the epistaxis was in fact responsible for death. I myself know of five such cases and conversation with medical officers in municipal and other hospitals where the elderly are catered for supports my conviction that spontaneous bleeding from the nose may be a problem worthy of serious consideration.

I do not intend to discuss either the various common local causes of epistaxis or rare conditions such as traumatic intracranial aneurysms and hereditary telangiectasis, or general predisposing factors, except in so far as the latter influence our plan of treatment. My purpose is to examine the fundamental principles which should guide us in treating emergency epistaxis, and to inquire how far our students have appreciated these principles as shown by the current methods we find employed for dealing with a condition which is frequently encountered, always disagreeable, and possibly dangerous.

Epistaxis belongs to that class of case which Wilfred Trotter classified as a relative emergency in that wise address to medical students published in his collected papers under the title "Emergency".

> "There is probably no more ancient and deeply contrived function than the natural control of hæmorrhage, and its capabilities are truly astonishing. They are, however, often underestimated, because they demand the exact fulfilment of certain conditions which are frequently with the best of intentions made impossible. These conditions are that the pressure within the bleeding vessel should be kept low and that the site of the bleeding point should be absolutely at rest. It is odd how difficult it is to get this simple principle understood, and the simple instructions that follow from it rigorously carried out. Conscientious nurse and anxious relative will conspire, the one to wash and the other to feed, in spite of categorical orders that nothing must be done or given, and exceptions to this rule will be taken for granted unless expressly forbidden.
>
> We are concerned here only with principles, and I shall but mention the one concrete example of severe epistaxis. Supposing you wish to make a serious attempt in such a case to avoid the recognized but odious alternative of plugging the nose, and to give natural arrest a real chance, this is the procedure to follow. Prop the patient well up with a comfortable inclination to one side, arrange a

large pad of wool for him to dribble into, put a dental prop between the teeth, *forbid him to breathe through the nose or swallow*, and give a substantial dose of morphia. Only by mouth breathing and a complete cessation of swallowing can the bleeding area be given the necessary and almost infallibly hæmostatic rest."

Now I do not say that every patient whose nose bleeds should be treated thus. Epistaxis from Little's area can generally be controlled by pressure with thumb or finger from outside the nostril but we would do well to impress on instructors of first-aid and school teachers that laying the patient down with wet cloths over the nose does not fulfil any of the conditions that encourage arrest of bleeding, and by allowing blood to drip into the pharynx leads to continuous swallowing, and subsequent vomiting and restlessness. The type of case for which Trotter's recommendations are most valuable is the severe epistaxis in the patient with a high blood-pressure. Here the bleeding, as likely as not, comes from deep in the nose and if it is to be controlled by packing requires specialized tools and a degree of skill that the ordinary practitioner does not always possess.

Packing is often found crowded into the anterior part of the nose possibly in front of a septal spur or deflection while blood soaks through the pack and drips into the pharynx. It is easy for specialists with head lamp, nasal speculum and forceps to see that plugging reaches the bleeding point but how many of our students get skilful at this simple manœuvre before they go into practice?

A dilatable rubber plug such as Rose's bag made from rubber finger-stall and a soft catheter will do less damage to the nasal mucosa but it does not always make pressure on the bleeding point if this is high in the ethmoidal area or in the nasopharynx.

Even skilful plugging which controls the bleeding temporarily may not prevent recurrence after the pack is removed in patients with pathological changes in the vessel walls. I have found records of several such cases.

One man, of 47, plethoric and alcoholic, was brought in from the street with severe bleeding apparently from both sides of the nose. Both sides of the nose were plugged at once by a competent registrar with adrenaline gauze. There was a history of hypertension but on admission the blood-pressure was only 100/60. The nose and post-nasal space were plugged seven times in three days but the bleeding recurred with severity a short time after each removal of the pack in spite of morphia, hæmoplastin, vitamin K, and calcium gluconate. The patient was restless, anxious, coughing and spitting and it was only when a good night's rest was obtained by brandy and paraldehyde that the bleeding stopped.

Another man of 45 who had been bleeding for four days before admission when he was found to have only 2,000,000 red cells and a hæmoglobin percentage of 46 did not stop bleeding in spite of daily packing for four days until he had blood transfusion. He was on the dangerously ill list for six days

I think we should examine the rationale of nose plugging in these cases in the light of the fundamental principles involved in the arrest of hæmorrhage. All the surgical measures used for controlling hæmorrhage, such as ligature and pressure, aim only at temporary arrest of the bleeding. Permanent arrest is a vital process the stages of which may be interrupted by sepsis as is seen in secondary hæmorrhage. That plugging the nose is productive of septic change is recognized by our insistence that no pack should be left in the nose for more than twenty-four hours. In patients with arterial disease where the muscular and elastic coats are converted into fibrous tissue, which prevents contraction and retraction of the vessel wall, thrombosis within and without the vessel must occur without hindrance as it is on clot formation alone that we can rely. Bacterial infection by means of its proteolytic ferments softens the newly-formed clot and allows the hæmorrhage to recur afresh. I believe that in patients with arterial disease it is particularly important not to disturb the natural defensive mechanism by which clotting occurs and to aim at securing hæmostatic rest by the method which Trotter advocates. Here are some notes of a case where this was satisfactorily obtained.

The patient was a woman of 35 with malignant hypertension whose blood-pressure was normally 250/150. She had a sudden massive epistaxis losing about two pints of blood. When examined by the registrar four hours later she was still bleeding freely anteriorly and posteriorly but no bleeding point could be seen. She was faint and cold with a rapid pulse and a B.P. of 190/140. She was given morphia and propped up in bed as described with a cork between her teeth. She felt dizzy for a short time, but when the registrar returned to the ward half an hour later he found the patient fairly comfortable and the bleeding stopped. He saw the patient hourly; the blood-pressure rose to 200/145 in three hours when the cork was removed. No further bleeding occurred. Another patient, a woman of 58 with a B.P. of 220/130, was found to have a pressure of 130/90 after six hours profuse epistaxis. She was treated in the same way. After an hour the bleeding had stopped completely and the B.P. was rising until three hours later it had risen to 170/100 but in spite of this no further bleeding occurred.

Not all the cases are as simple and dramatic as these and the patient who has been bleeding from the nose for several hours, who has been treated in a dilatory and ineffective manner may be so collapsed as to give rise to considerable anxiety.

I can recall an elderly patient seen many years ago, a known hypertensive, who, in spite of plugging, had been bleeding for thirty-six hours before admission. Packing temporarily controlled the hæmorrhage but it recurred each time the plug was removed. Finally the external carotid artery was ligatured under local anæsthetic. The patient died six hours later. (This operation was, I am afraid, action for its own sake which must be deplored.)

Wartime experience with blood transfusion has taught us that blood lost should be replaced. The old fear that transfusion, by raising the blood-pressure, will cause the bleeding to start again is not borne out by experience with drip methods. Indeed, it may be necessary to raise blood-pressure to save life. The collapsed hypertensive suffers the greatest risk under these conditions. The fatal case I have just mentioned had a B.P. of 110/80 on admission. There was a history of hypertension and, post mortem, generalized atherosclerosis was found. Such a patient should have a drip transfusion combined with the general measures advocated by Trotter. The restlessness and anxiety which are a prominent feature in the clinical condition of the patient who has lost much blood are quickly allayed with blood transfusion and morphia, far more effectively than with morphia alone. This was brought home to me forcibly during the war when for a time I was responsible for the ear, nose and throat work of a neighbouring Italian P.o.W. hospital in North Africa. The Italian habit of continuous coughing, hawking and spitting after any nose or throat operation quickly brought on hæmorrhage which increased the patient's agitation and restlessness, and set up a vicious circle which morphia did not control. It was only when I began giving a drip transfusion at a much earlier stage that this post-operative complication ceased to give me and the patient needless anxiety.

I do not think anyone now maintains (except to reassure his patient) that epistaxis with high blood-pressure is a safety-valve mechanism which should be allowed to pursue its course unchecked. If the physician wishes to reduce the blood-pressure by blood-letting he does it deliberately and under the control of B.P. estimations. Epistaxis is always distressing to the patient and worrying to the doctor but if the situation is handled in the way I have described, the bleeding that occurs will be beneficial to the patient and will cease before the blood loss has reached a dangerous level.

In conclusion I must refer to the value of these principles for the control of post-operative nose-bleeding. I think the most important practical point is the prevention of swallowing, i.e. the dental prop or cork between the teeth. Here is one example.

A man of 56 with a B.P. of 210/120 bled profusely from the left side of his nose on return from the operating theatre after bilateral removal of polypi and opening of the ethmoidal cells. When the registrar saw him his blood-pressure was 135/90. He was propped up, leaning on a bed-table, given morphia, reassurance and a dental prop. The bleeding soon ceased.

If the practitioner or house officer is taught to understand the principles which underlie the control of hæmorrhage, adequate treatment will be instituted at the onset of symptoms; and there will be fewer instances of intractable hæmorrhage calling for arterial ligature.

Anterior Ethmoidal Hæmorrhage

By R. G. MACBETH

AT the May Meeting of this Section in 1945 (*Proc. Roy. Soc. Med.* **38**, 620) I drew attention to the value of ligation of the anterior ethmoidal artery in certain cases of epistaxis. Since that time there have appeared reports of single cases by Reading (1945) and by Williams (1945), and an article by Weddell, Macbeth, Sharp and Calvert (1946). In this article we discussed the anatomy of the blood supply to the nasal cavities and described seven cases where severe epistaxis was controlled by this operation. (One of these cases was that reported by Williams, and culled by us from the records of a Military Hospital for Head Injuries.)

ANATOMY

As Miss Collier has said most cases of epistaxis cease spontaneously, or can be controlled readily without operation.

Severe epistaxis can be one of the most troublesome emergencies with which we in this Section are called upon to deal, and most of us can recollect anxious times when we have striven unavailingly to control such cases by repeated packing, cauterizations and transfusions. Ultimately, we may have ligated the external or common carotid artery, rather as a last resort, and in a number of cases this will have apparently succeeded in stopping the blood-flow. The majority of us, I think, have become obsessed by the idea that such epistaxis originates of necessity from an artery whose ultimate source is the external carotid system, and have forgotten that an important area of the nose is supplied ultimately from the Circle of Willis.

On an anatomical basis, therefore, we may divide epistaxis into two groups, depending upon whether it originates from the area of supply of one or the other of these main arterial systems. My colleagues and I have sought in vain in the literature for an appreciation that this point may be clinically important, and the remaining three of us owe a debt of gratitude to Dr. Weddell for pointing out why ligation of the external carotid sometimes fails in its object.

While the branches of the sphenopalatine and ethmoidal arteries anastomose freely on and in the lateral nasal walls and the septum, the former on the whole supplies the lower and more posterior parts of the cavity, and the latter supplies the upper and more anterior parts. It is also easy to understand why severe hæmorrhage occurring occasionally after antral operations is readily controlled by carotid ligature, while that occurring after an ethmoidectomy may not be controlled.

The middle concha is a convenient landmark whereby we may determine the ultimate source of bleeding, and it is usually possible during an epistaxis to get some idea as to whether the bleeding originates from above or below this structure, in front of it or behind. When such an observation has been made, and when carotid compression has been tried, and assuming that simple remedies have failed, the operative course of action should be clear. Either the external carotid or the anterior ethmoidal should be tied. We can see little point in ligating the internal maxillary artery via the transantral approach, as recommended by Hirsch (1936) and by Davis (1939), when the external carotid is so easy of access. They have suggested that failure of carotid ligation to control nasal bleeding, has been due to anastomosis of vessels across the mid-line; in our experience if carotid ligation fails the reason is that the wrong arterial system has been interrupted, and in such cases ethmoidal interruption succeeds. The difficult cases from the point of view of diagnosis are those where the bleeding appears to come from the region of anastomosis of the two arterial systems.

TYPES OF CASE

(*a*) *Injury*.—In cases of head injury there is often a fracture through the ethmoid, or through the fronto-ethmoidal suture, and this may involve the anterior ethmoidal artery or one of its main branches. These vessels lie in bony canals where they are subject to mural laceration or erosion, and where consequently they are unable to contract and retract. Thus, although they are quite small, the hæmorrhage to which they may give rise is often considerable.

In these cases bleeding may be immediate or at an interval after the original accident—i.e. it may be secondary in type, and presumably initiated by infection. Four of our cases occurred after injuries; in three of them carotid ligation had failed to stop the bleeding, and ethmoidal ligation succeeded. In the fourth this latter operation was undertaken with success as the primary and only operative measure.

I will quote two cases:

(1) F/O. S., aged 24, was involved in an air-crash in August 1944. There was hæmorrhage from the left nostril, but this subsided spontaneously. Eleven days later he had a profuse hæmorrhage; he was transfused and the nose was packed. Next day he bled again and it was noted that the bleeding originated in the olfactory cleft. Packing the nose again controlled him. Whenever the packing was removed, however, he bled profusely and had to be transfused.

The external carotid artery was exposed in the neck and tied; at that moment he coughed and expelled his packing and bled violently. The internal and common carotid arteries were then tied but this failed to diminish the bleeding. His nose was again packed and he was transfused.

Next day his nasal packing became loose and bleeding recommenced, and he was kept alive by continuous transfusion. I saw him for the first time at this stage, by which time he had received 18 pints of blood, and was losing it more rapidly than he was receiving it. After removal of the loosened pack, it was possible to confirm that the bleeding originated in the olfactory cleft; the pack was replaced and the anterior ethmoidal artery and a small accessory vessel were occluded by means of a silver clip. The pack was immediately removed, the patient bled no more, and made an uninterrupted recovery.

(2) J. B., aged 12, was struck on the nose by the leg of a chair early in July 1945. There was slight bleeding from the left nostril. Four weeks later he had his left antrum washed out by a colleague in London because of infection. Soon afterwards he went on a Thames camping holiday and on August 14, received a trivial injury to the nose from his sister. He seems to have bled a good deal into the punt, and it was only next day that he saw a doctor who packed the nostril. He came into hospital, the packing was removed, and there was no bleeding. Radiography revealed a fracture into the left frontal sinus and ethmoid.

Next day he bled again from the olfactory cleft, though not severely. The anterior ethmoidal artery was occluded under local anæsthesia, and the fracture was found to be actually involving the artery. There was no further bleeding.

(*b*) *Post-operative*.—These are really only special varieties of injury, and here sepsis is particularly likely to play a part. In such cases especially is packing not only likely to prove ineffective, but also actually dangerous because of the risk of meningitis.

I will quote one such case which, although it occurred in 1929, impressed itself vividly on my memory because of the number of nights of sleep I lost as a house surgeon in dealing with it.

A young R.A.F. officer had a submucous resection and middle turbinectomy. His post-operative period was uneventful, but on the eighth day after the operation he was taking a swing with a golf club, when he had a severe epistaxis and fainted. He returned to hospital with a nasal pack, which controlled him. Then there occurred a dreary period of treatment, when he had repeated epistaxes from the ethmoid region, always controlled by packing, but always recurring sooner or later after removal of the pack. He was transfused several times, and his external carotid and then his common carotid were tied unavailingly. He ultimately died from bronchopneumonia after the anæsthetic for the last ligation. I submit that he would have been saved if his anterior ethmoidal artery had been ligated.

(*c*) *Hyperpiesis.*—Hæmorrhage may occur from the area of the sphenopalatine artery in patients with hyperpiesis, and be readily controllable. But I believe that many of the cases in which the bleeding point is not readily found, but which is often "somewhere high up in the nose" belong to the anterior ethmoidal group, and I believe in such cases early ligature of that vessel would in many cases cut short what is often tedious treatment. One of our cases probably belonged to this group. Here this operation was the primary, only, and successful treatment after packing had failed, and the patient's Hb% had fallen to 38.

(*d*) *Idiopathic*—i.e. cases in which the cause can only be surmised or is never discovered, and where the bleeding comes from high up in the olfactory cleft. Two of our cases belonged to this group. In the one of them carotid ligation had failed; and in the other the patient was presumed to be suffering from telangiectasis of pregnancy, and when repeated packing failed, ethmoidal interruption was immediately successful.

TECHNIQUE

Anæsthesia.—Local infiltration by procaine or nupercaine is the method of choice; general anæsthesia is to be avoided because of the danger of aspiration of blood into the lungs. Infiltration and incision proceed as for external ethmoidectomy. The periosteum of the orbit is elevated from its medial wall to a depth of about 1¼ in. from the nasal bridge, when the ethmoidal vessels will be seen passing in a cuff of connective tissue to the foramen in the fronto-ethmoidal suture. Retraction of the orbital contents defines the vessels, and a silver clip is applied to them. Any accessory vessels and the posterior ethmoidal vessels can be coagulated with diathermy needle, or simply clamped and torn across (indeed diathermic coagulation may be all that is needed in the case of the main artery).

REFERENCES

DAVIS, E. D. D. (1939) *Brit. med. J.* (i), 721.
HIRSCH, C. (1936) *Arch. Otolaryng.*, 24, 589.
READING, P. (1945) *Brit. med. J.* (ii), 848.
WEDDELL, MACBETH, SHARP and CALVERT (1946) *Brit. J. Surg.*, 34, 387.
WILLIAMS. J. L. D. (1945) *J. Laryng.*, 60, 292.

E. D. D. Davis remarked on the surprising lack of knowledge on the physiology of the blood circulation of the nose. Very little was known about the type of condition seen in the elderly patient who started to bleed in the early morning, the bleeding continuing for four or five days and then spontaneously ceasing. It was a fallacy to treat such patients lying down; they should be sitting up. He quite agreed that the bleeding point should be attacked, but he had grave doubts whether ligature of the external carotid artery was of any value at all. The difficult cases were those which arose from injury, and it was in these that one might be called upon to tie the anterior or posterior ethmoidal artery. The cases were rare—he had had only two of them in his life. He tied the posterior ethmoid as well as the anterior.

One case was that of a young soldier who bled through the night, following a blow on the bridge of the nose which ruptured the anterior ethmoidal artery, and in spite of plugging and transfusion he died of hæmorrhage. In another case there was an arteriovenous aneurysm of the internal carotid artery as a result of a fractured skull following a motor-cycle accident. The common carotid artery was ligatured but the epistaxis was repeated forty-eight hours after the temporary arrest following the ligature.

H. V. Forster recalled an occasion when he had to deal with an injured seaman in mid-Atlantic. Severe nose bleeding presented a desperate problem, which, however, was solved, after washing out the nose, by packing with ribbon gauze soaked in compound tincture of benzoin, a method recommended by the late Dr. Ballinger of Chicago. Adrenaline impregnated gauze had become very foul in situ but the benzoin preparation did not and was retained with success for two to three days.

A late senior medical colleague of his suffered from intermittent nose bleeding, but a period of two years' observation passed before he was actually seen in an attack. The source being the ethmoid area to which a small pack was applied with permanent success.

In severe cases needing a choanal pack by the post-nasal route, a piece of tethered sorbo rubber sponge served very well, but in very nervous subjects small tethered pieces of this material could be passed one by one through the desensitized nasal passage into the nasopharynx and then gently drawn forwards as a group to fill the choana.

E. J. Gilroy Glass: I would like to draw attention to the necessity for routine cleansing of the nose, and removal of blood clot after nasal packs have been removed. Until this has been done the patient must be instructed not to inspire through the nose lest he dislodge a clot.

This danger was illustrated by a case in Nottingham just before the war. The patient was brought to hospital with his nose already packed. When the pack was removed bleeding had ceased, but there was still some clot in the nose. While the house surgeon was preparing to remove the clot, the man inspired forcibly through the nose and dislodged a large post-nasal clot, which entered the trachea and blocked both bronchi. Death supervened in a few seconds—long before any steps could be taken to remove the clot.

This cause of death may be an unusual one following epistaxis but it is preventable if the danger is realized.

L. Graham Brown said that packing the nose, after desensitizing, was the most important factor. Provided one did that first of all after irrigating the nose, by packing in a strip of cotton-wool soaked in 10% cocaine, it was comparatively easy, and usually successful. This was so much so that in most instances one could readily see any bleeding from the anterior septal area, or, if this was not the case, one could conclude that it was either higher up in the nose, or posteriorly. In the latter case one needed only to pack back on to the anterior surface of the sphenoid. He advocated the use of the narrowest ribbon gauze, namely, ¼ in. Widths of 1 in. or ¾ in. gauze could not be packed successfully. With the ¼ in. one got control, and this control could be confirmed by looking into the mouth to see if any bleeding continued to run down below the level of the soft palate.

Even in cases of new growth and in post-operative conditions, his experience had been that these vessels had to be tied very rarely indeed. He agreed with Miss Collier when she said that most cases could be controlled by direct pressure. In an external ethmoidectomy, for example, one did not bother very much about tying the anterior or posterior ethmoidal artery. Only in cases of trauma where the bone might be fractured and where the bleeding went on for some other reason did he see the need for tying these vessels. Again, in cases of new growth he had found that diathermy controlled the hæmorrhage sufficiently. In post-nasal pharyngeal tumours he had made use of a marine sponge packed into the nasopharynx and kept firmly in place by tapes passing out through the anterior nares, and with this in place for twenty-four hours, copious hæmorrhage, from the nasopharynx, after removal of a nasopharyngeal tumour, had been controlled. It was necessary to teach students, house surgeons, and general practitioners, if possible, that desensitization of the nose as a preliminary to packing made the latter a comparatively simple procedure.

Michael Vlasto said that when a condition of hyperpiesis was present, he had always considered it wise to refrain from any precipitate attempt to stem the epistaxis. He recalled a circumstance many years ago, when a senior anæsthetist with a high B.P. developed a severe epistaxis. In what he later regarded as an excess of enthusiasm, the epistaxis was effectively stemmed. A few days later the patient died of intracranial hæmorrhage.

Eric Watson-Williams said that he had had two cases of hyperpiesia in which treatment for nasal bleeding was disastrous. He thought there must be solid ground for the view that nose-bleeding was a safety valve in hyperpiesia.

T. B. Jobson said that he had a patient, a lady of 70, who had nose-bleeding about every month. An application of radium was made, and she remained free for six months, but after that the bleeding started again. He would welcome opinions on the advisability of further radium treatment.

CASES

Choanal Atresia.—T. M. Boyle.

T. M. Boyle said that he presented this patient for advice. She had suffered from nasal obstruction all her life. She had had two previous operations.

L. Graham Brown said that he had had experience of these cases, not only unilateral but bilateral. His procedure was to do a septal operation first and remove the posterior border of the septum. This allowed sufficient facility for the opening one was going to make. He made the opening with a suitable instrument, very often using the old-fashioned frontal sinus rasp. The bony opening was enlarged in that way on the outer side of the posterior choana. The other method was to put in a circular tube through the nose and out through the mouth, and keep rotating it for a period of ten days or more. The important point in the former method was to take away the bony posterior portion of the septum.

The President said that he entirely agreed with Mr. Brown as to the importance of removing the posterior part of the septum. He had operated on only two cases, one of which was a success.

E. D. D. Davis said that he would remove a little of the hard palate as well, because in these cases of atresia the floor of the nose came up almost to the body of the sphenoid.

Pemphigus of Pharynx.—H. S. Sharp.

Mrs. B., aged 65. She was seen at hospital on 11.10.46, complaining of sore throat for one month, following extraction of teeth. Blebs and blisters started on both shoulders at the same time. No previous attacks and no significant past illnesses. Examination showed pemphigus affecting soft palate, pharynx, left side of tongue and left buccal mucous membrane. The left arytenoid was also affected and left pyriform fossa contained mucopurulent fluid. The blebs on her arms were those of pemphigus. W.R. negative. Throat swab: no pathogenic organisms. Blood-count: R.B.C. 5,750,000; Hb 94%; C.I. 0·82; W.B.C. 7,800 (polys. 72%, eosinos. 1%, basos. 0, large monos. 3%, lymphos. 24%).

E. D. D. Davis said that he had gained the impression that the incidence of pemphigus had increased. All the cases presented the same sort of feature, that is to say, little blisters first of all on the soft palate, and then on the mucosa of the check, and again on the edge of the epiglottis. These blisters would break down, and little yellow sloughs would appear and disappear leaving a raw area which became painful. He had a doctor under his care with severe pemphigus of the mouth and chest. He had salvarsan, penicillin, various drugs from America of different descriptions. Of local applications, sulphathiazole powder did not help him. What *did* relieve him was aspirin-phenacetin mixture and painting the painful surface with pure carbolic.

Gummatous Destruction of Nasal Septum: Perforating Epithelioma of Nose.—H. S. Sharp.

Mr. J. D., aged 52, married, with one child. He was a brewer's employee. There was no history of primary specific infection or significant past illnesses. He had a cleft palate in youth. He was first seen at Charing Cross Hospital on 16.8.46 complaining of rapidly growing "spot" on nose. He had had nasal discharge and crusting off and on for years. The appearance was that of complete destruction of nasal septum and a perforating ulcer of nasal soft tissues. W.R. was positive (titre 60+). Biopsy of ulcer margin showed epithelioma grade I, with heavy infection.

An Aid to Swallowing after Laryngo-Pharyngectomy for Post-Cricoid Carcinoma (*Patient and prosthesis shown*).—H. A. Kidd.

Mrs. E. H. S., aged 54. Admitted to St. Helier's Hospital on 18.6.46 with a history of dysphagia and aphonia. She had been in bed for one week before admission to hospital. Considerable loss of weight. Stridor present.

Past history.—Left mastectomy eight years ago for, probably, benign condition.

On examination.—Thin, wasted patient. No glands palpable in neck. X-ray of chest negative. Laryngoscopy showed ulceration of the posterior part of the arytenoids and fixation of the cords in adduction. The blood-pressure was 162/105.

Operation (22.6.46).—Anæsthesia—local infiltration of decicain and adrenaline. Total laryngo-pharyngectomy was performed, and only two enlarged glands were found on the right side when block dissection of glands was carried out. Blood transfusion 2 pints. The specimen showed squamous celled carcinoma which extended downwards in the mucosa of the œsophagus for 2 in. Microscopic section of the glands did not show any malignant deposits.

Post-operative treatment.—Penicillin injections and sulphathiazole. Feeds through œsophageal tube.

Convalescence uninterrupted. Discharged from hospital on 7.7.46.

A Gluck's tube was found to be unsatisfactory, and the prosthesis now being worn was made by Mr. Arthur Bell, L.D.S., and has enabled the patient to swallow her saliva without leak, and to take liquids and semi-solids. The prosthesis was modelled in plaster of Paris and then made of acrylic resin. It is attached to a 4 in. rubber tube and passes down the œsophagus and acts as a fitted funnel to the œsophagus. It collects the food as it passes over the skin between the pharyngeal stoma and the lower cut end of the œsophagus. Unlike the Gluck's tube it does not attempt to fit into the irregular and constantly altering shapes of the pharyngeal stoma.

Lionel Colledge said that the apparatus seemed to work very well in Mr. Kidd's patient. He had never found any eventual difficulty with Gluck's tube if one had several sizes made and cut them carefully, but recently the rubber was of poor quality. He did not have many cases of this sort nowadays: they were treated by radium. Some figures were published in the Lettsomian Lectures of the Medical Society of London three years ago. He thought that with regard to this particular patient the only thing left for her was to have some radiotherapy. Some cases which had had recurrences over several years had been improved and sometimes apparently permanently healed after radiotherapy.

E. Musgrave Woodman congratulated the exhibitor on the apparatus he had supplied for his patient which seemed to work extremely well. Was it not possible to deal surgically with the small recurrent area? If the further portion of that substance could be taken away surgically, even if a certain amount of deformity resulted, it was better than depending on radiotherapy. In that area radiotherapy produced a transient improvement rather than a radical cure.

Recurrent Chondroma of the Subglottic Region.—F. C. W. Capps.

E. W. A., male, aged 74.

On examination.—First seen in April 1937 complaining of six months' hoarseness. Slight inspiratory stridor. On laryngoscopy, had smooth swelling in the subglottic region which appeared to surround the whole lumen, but was most marked on the posterior aspect. Direct laryngoscopy, and high tracheoscopy showed a hard smooth swelling about ½ in. from back to front and 1 to 1½ in. deep on the posterior wall of the trachea. A piece was removed for examination. There was no bleeding.

Pathological report.—Tumour is a chondroma which is ossifying in parts, and also shows areas of calcification. Some of the fragments show much fibrino-purulent material on the surface. The tumour does not appear to be malignant.

Operation (26.4.37).—Anæsthetic—Gas and oxygen through tracheotomy tube. Laryngofissure and opening of the upper part of the trachea. The tumour, lying in the posterior wall of the larynx below the vocal cords was defined. It was found to have an irregular surface; to be moderately soft with cartilaginous areas in parts. This mass was removed by curetting with a sharp "Volkmann's spoon", leaving the post-laryngeal wall fairly clean. Throughout the operation care was taken to prevent any blood from going down the trachea. The wound was packed with flavine gauze which was brought out above a large tracheotomy tube. The larynx closed by Michel clips. Recovery was uneventful.

When seen again in June 1946 was found to have hard nodular swellings on both sides of the scar in the neck. The left cord was fixed; the right showed limited abduction. He has an adequate airway if he is careful.

H. V. Forster said that many years ago a doctor friend came to see him for loss of voice. There was immobility of one cord. The patient came to London later and was operated on by the late Sir James Berry. Its cause proved to be a chondroma. The growth had not been approached by laryngofissure which he thought was a route favoured by laryngologists.

Persistent Epiphora following Acute Dacryocystitis.—Brian Reeves.

This case had had a dacryocystorhinostomy and was shown to demonstrate an alternative approach to the lacrimal sac and duct. The patient's epiphora had subsided completely and the scar of the operation was almost invisible. The lacrimal duct was exposed as in Norman Patterson's external sinus operation. The somewhat extensive exposure was justified by the ease and accuracy with which the anastomosis could be made into the atrium of the nose. After the operation was completed a loop of nylon was threaded through the punctum into the nose, the two ends were tied and left in situ for seven days.

Slides were shown to demonstrate the steps of the operation.

L. Graham Brown said that a number of these cases could be done intranasally, especially with a wide nose. If one could see the sac made obvious by a stylet passed down the sac from above, one could take out a snippet with a suitable instrument and by irrigation of the lacrimal sac maintain patency into the nose. He congratulated the President and Mr. Reeves on an excellent result, but he thought it was an elaborate technical operation which in many cases was not necessary.

The President said that he had tried in several cases what Mr. Graham Brown had just suggested, but the results were not satisfactory. Ophthalmic surgeons, he thought, were now favouring an external route of approach.

Brian Reeves also said that he had tried the intranasal operation but found it too difficult.

H. V. Forster said that Thomas Guthrie had described a method of delivering large pieces of nasopharyngeal fibroma through the nose by doing a resection of the pyriform aperture and some years ago a Scandinavian rhinologist had suggested approaching the lacrimal sac by this route and proceeding by submucous resection of the intervening parts.

He was grateful for the suggestion to pass a nylon strip to keep the lacrimal channel patent.

days or more. The important point in the former method was to take away the bony posterior portion of the septum.

The President said that he entirely agreed with Mr. Brown as to the importance of removing the posterior part of the septum. He had operated on only two cases, one of which was a success.

E. D. D. Davis said that he would remove a little of the hard palate as well, because in these cases of atresia the floor of the nose came up almost to the body of the sphenoid.

Pemphigus of Pharynx.—H. S. Sharp.

Mrs. B., aged 65. She was seen at hospital on 11.10.46, complaining of sore throat for one month, following extraction of teeth. Blebs and blisters started on both shoulders at the same time. No previous attacks and no significant past illnesses. Examination showed pemphigus affecting soft palate, pharynx, left side of tongue and left buccal mucous membrane. The left arytenoid was also affected and left pyriform fossa contained mucopurulent fluid. The blebs on her arms were those of pemphigus. W.R. negative. Throat swab: no pathogenic organisms. Blood-count: R.B.C. 5,750,000; Hb 94%; C.I. 0·82; W.B.C. 7,800 (polys. 72%, eosinos. 1%, basos. 0, large monos. 3%, lymphos. 24%).

E. D. D. Davis said that he had gained the impression that the incidence of pemphigus had increased. All the cases presented the same sort of feature, that is to say, little blisters first of all on the soft palate, and then on the mucosa of the cheek, and again on the edge of the epiglottis. These blisters would break down, and little yellow sloughs would appear and disappear leaving a raw area which became painful. He had a doctor under his care with severe pemphigus of the mouth and chest. He had salvarsan, penicillin, various drugs from America of different descriptions. Of local applications, sulphathiazole powder did not help him. What *did* relieve him was aspirin-phenacetin mixture and painting the painful surface with pure carbolic.

Gummatous Destruction of Nasal Septum: Perforating Epithelioma of Nose.—H. S. Sharp.

Mr. J. D., aged 52, married, with one child. He was a brewer's employee. There was no history of primary specific infection or significant past illnesses. He had a cleft palate in youth. He was first seen at Charing Cross Hospital on 16.8.46 complaining of rapidly growing "spot" on nose. He had had nasal discharge and crusting off and on for years. The appearance was that of complete destruction of nasal septum and a perforating ulcer of nasal soft tissues. W.R. was positive (titre 60+). Biopsy of ulcer margin showed epithelioma grade 1, with heavy infection.

An Aid to Swallowing after Laryngo-Pharyngectomy for Post-Cricoid Carcinoma (*Patient and prosthesis shown*).—H. A. Kidd.

Mrs. E. H. S., aged 54. Admitted to St. Helier's Hospital on 18.6.46 with a history of dysphagia and aphonia. She had been in bed for one week before admission to hospital. Considerable loss of weight. Stridor present.

Past history.—Left mastectomy eight years ago for, probably, benign condition.

On examination.—Thin, wasted patient. No glands palpable in neck. X-ray of chest negative. Laryngoscopy showed ulceration of the posterior part of the arytenoids and fixation of the cords in adduction. The blood-pressure was 162/105.

Operation (22.6.46).—Anæsthesia—local infiltration of decicain and adrenaline. Total laryngopharyngectomy was performed, and only two enlarged glands were found on the right side when block dissection of glands was carried out. Blood transfusion 2 pints. The specimen showed squamous celled carcinoma which extended downwards in the mucosa of the œsophagus for 2 in. Microscopic section of the glands did not show any malignant deposits.

Post-operative treatment.—Penicillin injections and sulphathiazole. Feeds through œsophageal tube.

Convalescence uninterrupted. Discharged from hospital on 7.7.46.

A Gluck's tube was found to be unsatisfactory, and the prosthesis now being worn was made by Mr. Arthur Bell, L.D.S., and has enabled the patient to swallow her saliva without leak, and to take liquids and semi-solids. The prosthesis was modelled in plaster of Paris and then made of acrylic resin. It is attached to a 4 in. rubber tube and passes down the œsophagus and acts as a fitted funnel to the œsophagus. It collects the food as it passes over the skin between the pharyngeal stoma and the lower cut end of the œsophagus. Unlike the Gluck's tube it does not attempt to fit into the irregular and constantly altering shapes of the pharyngeal stoma.

Lionel Colledge said that the apparatus seemed to work very well in Mr. Kidd's patient. He had never found any eventual difficulty with Gluck's tube if one had several sizes made and cut them carefully, but recently the rubber was of poor quality. He did not have many cases of this sort

Section of Physical Medicine

President—FRANK COOKSEY, O.B.E., M.D.

[*January* 8, 1947]

REHABILITATION IN CHEST INJURY

Mr. T. Holmes Sellors: Before it can be assumed that the surgeon's task is complete, the patient must be restored to mental and physical fitness. Certain branches of surgery have developed more adequately than others the control of the patient between the active phases of illness and his return to work, and among these chest surgery can claim to play an active part.

Some of the reasons for this lie in the fact that time taken for convalescence and re-education within the chest hospital or unit is on the whole very much longer than that obtaining in most aspects of general surgery. This time factor resembles more that of the sanatorium than the busy urban hospital, and even though there is no excuse for waste of time in a chest unit, experience has shown us that attempts to treat cases too often as out-patients have not met with adequate success. For example, in cases of chronic empyema, in which control of the dead space, cavity and tube is of the utmost importance, it has been found more economical in the long run to maintain these patients in hospital under observation until cure has been effected. This relatively long-term policy does not, however, become necessary in all branches of chest surgery, but exists in its most exaggerated form in surgical cases of tuberculosis and chronic chest suppurations. Many straightforward cases can be restored as virtually fit for their former occupations in the space of two or three months, but the difficult cases, as has been said, are those whose control may cover a period of one or even two years. It is to this latter group that most of the later comments will refer.

For convenience, any discussion on rehabilitation can be divided into two main sections—general and local—that is, the handling of the patient as a whole and the more local restoration of chest functions.

General.—The patient, on admission to chest hospital or unit, may develop after some weeks or months a physical and moral lethargy which must be combated at every turn if the general condition allows. The necessity for maintaining chest cases in bed for a long period is not usual, and most patients can be up and about for a considerable period of the day once the acute stages of illness are over. They should not be allowed to slouch around the wards in dressing gown and slippers, but should dress, wear shoes, and in general comport themselves as ordinary individuals. There is a great deal to be said for setting a certain routine—small tasks or jobs which help to fix the day's timetable; and a certain amount of physical exercise, walking in the hospital grounds, or even games may be permitted, so as to encourage muscular redevelopment and general body tone. There is no necessity to keep the patient within the hospital gates if the surrounding amenities permit of greater activities.

With the added freedom that obtains in a hospital in the country, there is a good case to be made out for the unit's location away from built-up areas, since the value of an open environment must inevitably play a considerable part in recovery.

Diet must be carefully planned. Some patients lose a lot of protein in their discharges, and this loss must be adequately replaced. The menu should be varied as the patient may be in the unit for months and the importance of variety and imagination in his diet must be considered.

The most difficult part of the general treatment, however, is the psychological aspect. The patient who is at first interested and energetic may easily become apathetic in a period of time, and deteriorate into that unfortunate state known as "hospitalization". This requires the utmost energy on the part of the staff to combat, and one looks forward to the day when the greater use of occupational

The President said that another method of approaching the duct was through the antrum. He had seen this route employed by a German surgeon. By the method here exhibited it was possible owing to the good exposure to see what one was doing.

Recurrent Papillomata and Webbing of the Larynx.—D. F. A. Neilson.

Man aged 49, who was gassed in 1918 and states that his voice has never been quite normal since then. In 1931-1940-1942 he underwent endolaryngeal operations for removal of papillomata and subsequent to the last operation he was given a course of deep X-ray therapy. Six applications over a period of six weeks. Total dosage 2000 r. Microscopic examination on several occasions revealed no evidence of malignancy. Two patches of papillomatous growth were removed from the upper surface of the web adhesion uniting the anterior thirds of the right and left cords. A large pedunculated papillomatous mass was removed from just below the left vocal cord, the size of a large pea. There was improvement for a time, but the patient has now relapsed and the papilloma below the cord has recurred along the under-surface.

The case was shown for suggestions as to re-treatment, and to demonstrate the danger of injury to the glottis being followed by adhesion of the edges of the vocal cords.

Congenital Bilateral Fistula of Tear Duct. One Side Treated by Toti's Operation.—J. F. Simpson.

The patient was a boy of 7. The lacrimal duct opened on the face about ¼ in. below the inner canthus. A thick mucopurulent discharge had exuded from these fistulæ since birth, and epiphora had been present. An X-ray examination with lipiodol injected into the fistulæ, showed a dilated duct and sac without drainage into the nose. The patent inferior canaliculi were well demonstrated. A right dacryocystorhinostomy was performed on November 22, with excision of the fistula. Epiphora had ceased on this side, and it was proposed to operate on the left side shortly. No bougies had been passed. The case was shown because of the comparative rarity with which such a congenital deformity was seen.

Osteoma of Nasopharynx.—A. W. McCay.

G. S., male, aged 46. Gradually increasing nasal obstruction on the right side for the past two and a half years. Right nostril now completely obstructed, the left partially. Hard bony tumour filling the right choana and partially obstructing the left. This bony mass can be palpated through the right nostril of which it appears to fill the posterior third. X-ray photographs show the bony mass but do not give any indication as to its site of origin.

EXHIBIT

Preliminary Model for an Indirect Laryngoscope.—W. O. Lodge.

The buccal portion is tubular. The pharyngeal spatula is mechanically depressed through a right angle by closure of the handle, taken from a Ballenger's guillotine. A siphon tube to warm the mirror is fitted. The lighting unit is detachable. The instrument can be sterilized by boiling. After other improvements in the design have been made, portions of the metal will be cut away to allow of the passage of instruments.

Section of Physical Medicine

President—FRANK COOKSEY, O.B.E., M.D.

[*January* 8, 1947]

REHABILITATION IN CHEST INJURY

Mr. T. Holmes Sellors: Before it can be assumed that the surgeon's task is complete, the patient must be restored to mental and physical fitness. Certain branches of surgery have developed more adequately than others the control of the patient between the active phases of illness and his return to work, and among these chest surgery can claim to play an active part.

Some of the reasons for this lie in the fact that time taken for convalescence and re-education within the chest hospital or unit is on the whole very much longer than that obtaining in most aspects of general surgery. This time factor resembles more that of the sanatorium than the busy urban hospital, and even though there is no excuse for waste of time in a chest unit, experience has shown us that attempts to treat cases too often as out-patients have not met with adequate success. For example, in cases of chronic empyema, in which control of the dead space, cavity and tube is of the utmost importance, it has been found more economical in the long run to maintain these patients in hospital under observation until cure has been effected. This relatively long-term policy does not, however, become necessary in all branches of chest surgery, but exists in its most exaggerated form in surgical cases of tuberculosis and chronic chest suppurations. Many straightforward cases can be restored as virtually fit for their former occupations in the space of two or three months, but the difficult cases, as has been said, are those whose control may cover a period of one or even two years. It is to this latter group that most of the later comments will refer.

For convenience, any discussion on rehabilitation can be divided into two main sections—general and local—that is, the handling of the patient as a whole and the more local restoration of chest functions.

General.—The patient, on admission to chest hospital or unit, may develop after some weeks or months a physical and moral lethargy which must be combated at every turn if the general condition allows. The necessity for maintaining chest cases in bed for a long period is not usual, and most patients can be up and about for a considerable period of the day once the acute stages of illness are over. They should not be allowed to slouch around the wards in dressing gown and slippers, but should dress, wear shoes, and in general comport themselves as ordinary individuals. There is a great deal to be said for setting a certain routine—small tasks or jobs which help to fix the day's timetable; and a certain amount of physical exercise, walking in the hospital grounds, or even games may be permitted, so as to encourage muscular redevelopment and general body tone. There is no necessity to keep the patient within the hospital gates if the surrounding amenities permit of greater activities.

With the added freedom that obtains in a hospital in the country, there is a good case to be made out for the unit's location away from built-up areas, since the value of an open environment must inevitably play a considerable part in recovery.

Diet must be carefully planned. Some patients lose a lot of protein in their discharges, and this loss must be adequately replaced. The menu should be varied as the patient may be in the unit for months and the importance of variety and imagination in his diet must be considered.

The most difficult part of the general treatment, however, is the psychological aspect. The patient who is at first interested and energetic may easily become apathetic in a period of time, and deteriorate into that unfortunate state known as "hospitalization". This requires the utmost energy on the part of the staff to combat, and one looks forward to the day when the greater use of occupational therapy will be able to interest patients to a far wider extent than is possible at the present, when materials and staff are limited. Occupational therapy should not aim at being a commercial proposition. It should be an adequate relaxation with a certain amount of mental and manual exercise for the patient, though it is admitted that on some occasions the patient may find himself in later times more suited to a job which had its base in the occupational therapy he learned in the hospital. The prime object is, however, to aim at returning patients to their original vocation, and to encourage their activities in such a way that the change over from hospital to normal economic life is not too sharp.

The degree of psychological and emotional stress produced by the economic position is a further point that is not dealt with sufficiently fully. The invaluable work of hospital almoners and others helps to mitigate hardship, but often, though the pecuniary loss to the family may not be the main factor, the man's worries require most sympathetic and comprehensive handling.

Local.—The much more technical aspect of rehabilitation for the thoracic worker is concerned with actual chest functions. The effect of most thoracic diseases is to diminish chest movements, and to leave the thorax and therefore the lung in a contracted position. The chest becomes flattened and scoliosis may develop rapidly (fig. 1). The ribs become approximated and rigid, leading to diminished movement and function.

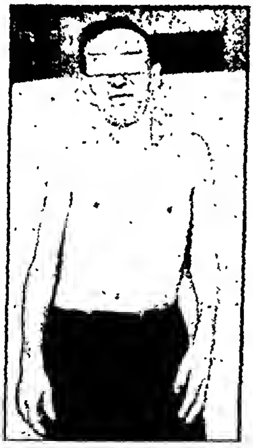


FIG. 1.

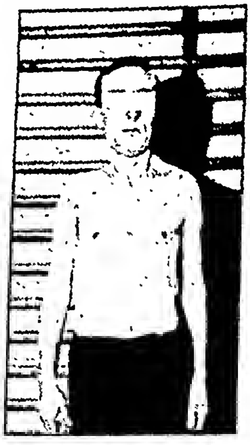


FIG. 2.

FIG. 1.—Posture and deformity following infected hæmothorax (left). The upper ribs and part of the brachial plexus were damaged. The chest was drained.

FIG. 2.—After three months' treatment considerable improvement has been obtained. The empyema is not yet closed.

The comments under this heading for convenience will be confined to chronic empyema, whose treatment illustrates most of the features that will be discussed.

Some degree of chest contraction and deposition of fibrin on the pleural surfaces can occur quite rapidly, but the remedy and restoration of movement may take a long time. It is therefore absolutely essential to institute treatment as early and energetically as possible. It may be assumed that where the chest wall moves freely and actively the underlying lung will be functioning efficiently, and similarly should lung function be lost subsequent contraction of the chest is almost inevitable.

The active movements of the chest must be instituted by the efforts of the patient himself, and started at the earliest possible moment, to be continued through the whole period of treatment and well into normal life. Only in this way can we hope to regain that full function which disease may have abolished.

From the medical and nursing point of view there are certain important details to be observed. Circular bandages or constricting dressings must be avoided, and in bed the posture of the patient requires to be watched continually. In bed in the semi-sitting position the patient tends to develop a marked kyphosis, and frequently slumps towards the affected side, exaggerating his deformity and producing scoliosis.

The exercises to re-establish chest movement are essentially based on *inspiratory* efforts. The old idea of using blowing efforts to aid re-expansion of lung are almost valueless and should not be employed. The active inspiratory exercises that have been devised depend on the establishment of energetic and localized movement of the part of the chest wall indicated. The physiotherapist, having analysed the deformity or, in the case of an empyema, the area of the dead space, starts by making pressure with the hand over the chest wall, and encouraging the patient to expand and even actively push that hand away. After voluntary control has been established by the patient, these exercises can be undertaken without constant supervision but they should be continued not for minutes but for several hours each day. Lack of concentration and failure to persist cannot achieve a good result. The physiotherapist, treating an individual or a class, is there to see that the exercises are properly done, and to control the way and degree of expansion that is being obtained. It is up to the patient to put this into practice. These localized pressure cxpansion exercises are the work of a few pioneers, and the subject is far too little known from the practical aspect. My association with Miss Reed, Miss Thacker and others at Harefield has enabled me to judge what efficient results can be obtained by carefully devised and above all conscientiously controlled exercises.

In general the chest movements can be divided into two groups. The movement of the lower ribs both laterally and anteriorly are important, and also a certain amount of posterior expansion can be obtained. Furthermore there are the diaphragmatic movements which aid basal re-expansion to a great extent (fig. 6). At the apex the only effort that can be made for practical purposes is the anterior expansion (fig. 3).

There are several points that have to be observed in these breathing exercises apart from those already mentioned. These include maintaining the chest steady except for the area that is being exercised, and seeing that sufficiently firm pressure is made over that area while the inspiratory effort is being made. Broad webbing belts are also useful in concentrating the effort, and if these exercises are done in front of a mirror or in class some of the more common errors can be counteracted.

In some other conditions of chest surgery, such as thoracoplastic operations, breathing exercises on a less severe scale will be used to encourage the patient to make use of parts of the lung away from the operation area, and to increase the respiratory function. The question of posture of the patient is most important, and is incidentally one of the helpful reasons for having the patient out of bed. The traditional nursing arrangement of pillows in the form of a "V" is not always desirable, since it encourages kyphosis and prevents the patient holding himself in a good posture. Several pillows arranged across the patient's back are preferable to a "V"-shaped arrangement, and at all times we give the patient "the freedom of the bed" at the earliest possible moment (fig. 8).

The importance of coughing in chest diseases to eject sputum is more part of actual operative after-treatment than of rehabilitation, but if there is any sputum persisting after operation, then regular and purposeful coughing or even postural drainage must be instituted.

Thoracotomy incisions frequently divide some of the scapular muscles, and re-establishment of arm movement from the very early post-operative days is important (fig. 9). During the latter stages a continual check should be made to see that the arm is being freely and actively used if healing has been normal.

The regular measurement of the vital capacity is of considerable help both to

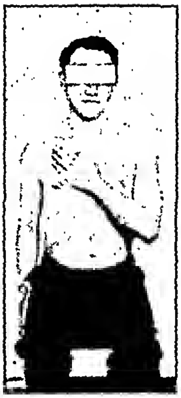


FIG. 3.

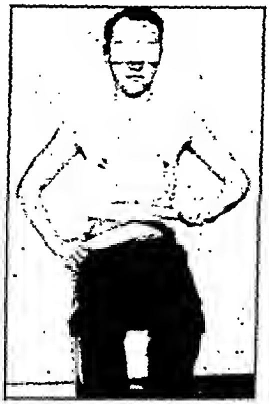


FIG. 4.

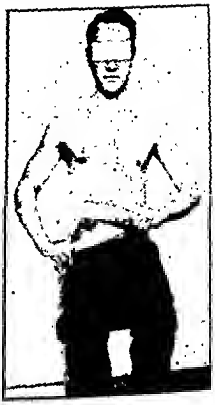


FIG. 5.

FIG. 3.—Apical expansion. Fingers are pressed against the upper ribs below the right clavicle. This helps to concentrate the inspiratory effort and movement.

FIGS. 4 and 5.—Lateral basal expansion (right). Use of belt which makes pressure against the ribs. Right hand is held still, while movement of the left hand demonstrates the degree of excursion obtained. Note absence of spine flexion. (4) Inspiration. (5) Expiration.

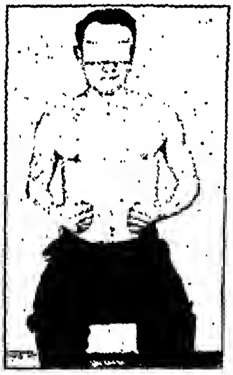


FIG. 6.—Localized expansion breathing exercises. Right empyema (Mr. Vernon Thompson's case). Diaphragmatic breathing: pressure is exerted in the costal margins by the knuckles as the abdominal wall is contracted and relaxed (inspiration).

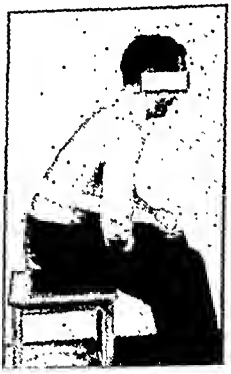


FIG. 7.—Posterior basal expansion. Use of belt with right hand stationary, and the left hand showing degree of movement obtained (inspiration).

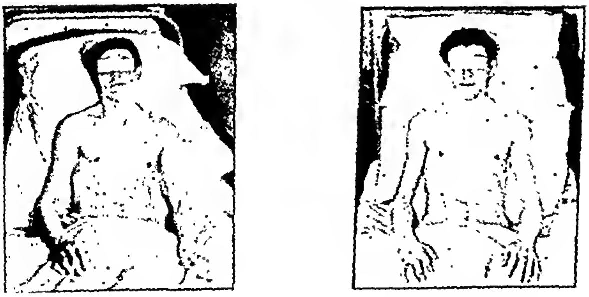


FIG. 8 (*a*). FIG. 8 (*b*).

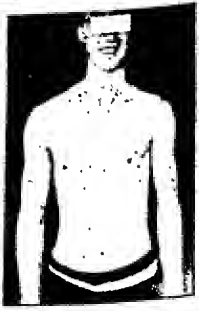


FIG. 9.

FIG. 8.—Posture in bed following thoracic operation. (*a*) Incorrect: showing kyphosis and lateral flexion of trunk. Note typical appearance of head and neck; pillows are badly placed. (*b*) Corrected position; spine straight, and the pillows placed firmly and horizontally behind the back.

FIG. 9.—Absence of chest deformity following left pneumonectomy for cystic bronchiectasis.

patient and staff, giving a measure of progress which, if not exact, is at any rate comparative, and along with this a routine clinical examination must be made.

Chronic pleural infections are liable to be followed by secondary anæmia, which may require treatment by drugs or even transfusion. It is, of course, important for the medical staff to encourage patients but at the same time to be firmly in control of their activities. It is easy to become casual in the case of prolonged illness, and it requires considerable effort from all parties concerned to maintain the necessary degree of enthusiasm and drive that should carry the patients through from their illness to a stage when they are virtually fit to return to the outside world and their former occupation.

A routine follow-up which includes radiological investigation is an important part of the control after the patient has left hospital.

On returning home the tendency to give up breathing exercises, or to adopt a faulty posture, is always there, and patients can be very like children who, under supervision, are admirably behaved, but when out of sight of their mentors tend to do the wrong things.

The return of the patient from hospital to his own or some other occupation is an interesting and critical feature as the end-result of our efforts in rehabilitation. In our own cases details have been handled by Dr. MacPhail.

Dr. William M. MacPhail: The essence of rehabilitation is good treatment. It is just good treatment made more complete and carried to its logical conclusion in restoring function as fully as possible and restoring the individual concerned to the working life of the community.

A self-contained speciality, such as a thoracic unit, provides an excellent opportunity for the essential team-work. Within the bounds of the unit there is ideal opportunity for co-operative work by the team of surgeon, physician, nursing staff and ancillary services. These ancillary services fall into three groups:—

(1) *Physiotherapists.*—Their work is so much a part of functional and indeed, mental, restoration after thoracic surgery, that the non-use of physiotherapy almost amounts to malpraxis in these days.

(2) *Occupational therapy* fulfils a useful purpose in arousing interest and initiative in patients who have had a long and discouraging illness. There should be more occupational therapy of a technical character, particularly for male patients, and the educational aspect of occupational therapy should be better developed. Along the educational line, we do a little at present, with the aid of correspondence courses, but to benefit fully from this the patient really requires some informed help and supervision. It would be more satisfactory to have in the hospital the services of a visiting educational officer. This is a very likely development of great value. Another possibility is the use of any near-by technical school or college where ambulant patients could there attend classes and receive useful technical training.

(3) *Almoners.*—As Mr. Sellors has pointed out the actual surgical operation itself is merely an incident in the course of hospital treatment of a given case. But in relation to the whole life of the individual concerned the hospital treatment is merely an incident. In order to appreciate the patient's difficulties during the time of illness and in order to make useful provision for the future, it is necessary to be intimately acquainted with the past. This is the great task of the almoners' department, and without their ceaseless interest and vigilance our rehabilitation programme would halt very badly.

The foregoing remarks apply to the rehabilitation of all patients undergoing treatment in a thoracic surgical unit. The majority of patients do not present a special problem with regard to their settlement in work. They return to their own occupation, or to their own homes if they are housewives.

With a number of patients, however, there is such a special problem in regard to employment, whether it be return to former employment on modified terms or finding a new job, or the taking up of an entirely new occupation. In regard to these cases presenting this problem of reorientation of life and of re-employment, I would like to make the following six suggestions:

(1) The approach to each case must be the individual approach. This is not a matter which can be handled by any mass tactics, or failure is certain. Each patient must be an individual study and must be constantly guided and helped till a satisfactory resettlement has been achieved.

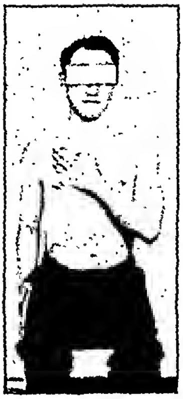


FIG. 3.

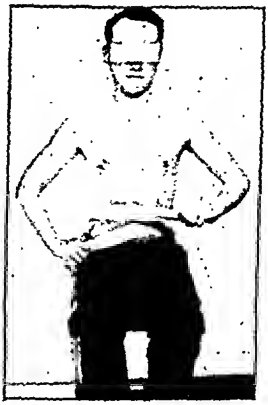


FIG. 4.

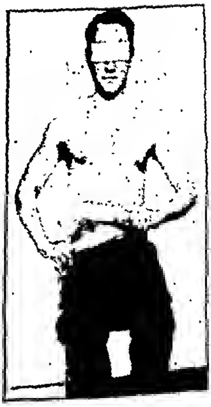


FIG. 5.

FIG. 3.—Apical expansion. Fingers are pressed against the upper ribs below the right clavicle. This helps to concentrate the inspiratory effort and movement.

FIGS. 4 and 5.—Lateral basal expansion (right). Use of belt which makes pressure against the ribs. Right hand is held still, while movement of the left hand demonstrates the degree of excursion obtained. Note absence of spine flexion. (4) Inspiration. (5) Expiration.

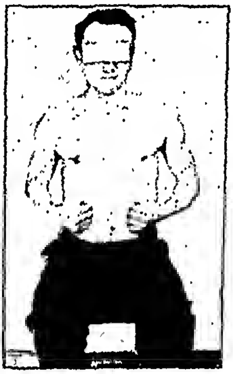


FIG. 6.—Localized expansion breathing exercises. Right empyema (Mr. Vernon Thompson's case). Diaphragmatic breathing: pressure is exerted in the costal margins by the knuckles as the abdominal wall is contracted and relaxed (inspiration).

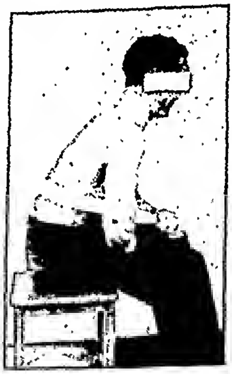


FIG. 7.—Posterior basal expansion. Use of belt with right hand stationary, and the left hand showing degree of movement obtained (inspiration).

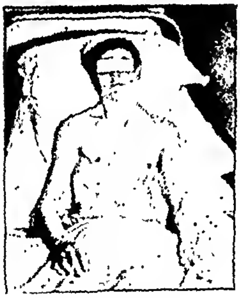


FIG. 8 (a).

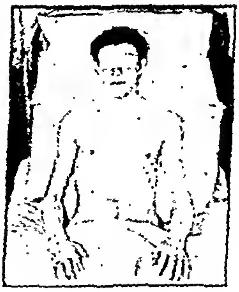


FIG. 8 (b).

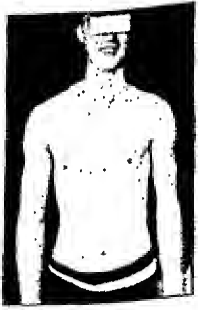


FIG. 9.

FIG. 8.—Posture in bed following thoracic operation. (a) Incorrect: showing kyphosis and lateral flexion of trunk. Note typical appearance of head and neck; pillows are badly placed. (b) Corrected position; spine straight, and the pillows placed firmly and horizontally behind the back.

FIG. 9.—Absence of chest deformity following left pneumonectomy for cystic bronchiectasis.

patient and staff, giving a measure of progress which, if not exact, is at any rate comparative, and along with this a routine clinical examination must be made.

Chronic pleural infections are liable to be followed by secondary anæmia, which may require treatment by drugs or even transfusion. It is, of course, important for the medical staff to encourage patients but at the same time to be firmly in control of their activities. It is easy to become casual in the case of prolonged illness, and it requires considerable effort from all parties concerned to maintain the necessary degree of enthusiasm and drive that should carry the patients through from their illness to a stage when they are virtually fit to return to the outside world and their former occupation.

A routine follow-up which includes radiological investigation is an important part of the control after the patient has left hospital.

On returning home the tendency to give up breathing exercises, or to adopt a faulty posture, is always there, and patients can be very like children who, under supervision, are admirably behaved, but when out of sight of their mentors tend to do the wrong things.

The return of the patient from hospital to his own or some other occupation is an interesting and critical feature as the end-result of our efforts in rehabilitation. In our own cases details have been handled by Dr. MacPhail.

Dr. William M. MacPhail: The essence of rehabilitation is good treatment. It is just good treatment made more complete and carried to its logical conclusion in restoring function as fully as possible and restoring the individual concerned to the working life of the community.

A self-contained speciality, such as a thoracic unit, provides an excellent opportunity for the essential team-work. Within the bounds of the unit there is ideal opportunity for co-operative work by the team of surgeon, physician, nursing staff and ancillary services. These ancillary services fall into three groups:—

(1) *Physiotherapists.*—Their work is so much a part of functional and indeed, mental, restoration after thoracic surgery, that the non-use of physiotherapy almost amounts to malpraxis in these days.

(2) *Occupational therapy* fulfils a useful purpose in arousing interest and initiative in patients who have had a long and discouraging illness. There should be more occupational therapy of a technical character, particularly for male patients, and the educational aspect of occupational therapy should be better developed. Along the educational line, we do a little at present, with the aid of correspondence courses, but to benefit fully from this the patient really requires some informed help and supervision. It would be more satisfactory to have in the hospital the services of a visiting educational officer. This is a very likely development of great value. Another possibility is the use of any near-by technical school or college where ambulant patients could there attend classes and receive useful technical training.

(3) *Almoners.*—As Mr. Sellors has pointed out the actual surgical operation itself is merely an incident in the course of hospital treatment of a given case. But in relation to the whole life of the individual concerned the hospital treatment is merely an incident. In order to appreciate the patient's difficulties during the time of illness and in order to make useful provision for the future, it is necessary to be intimately acquainted with the past. This is the great task of the almoners' department, and without their ceaseless interest and vigilance our rehabilitation programme would halt very badly.

The foregoing remarks apply to the rehabilitation of all patients undergoing treatment in a thoracic surgical unit. The majority of patients do not present a special problem with regard to their settlement in work. They return to their own occupation, or to their own homes if they are housewives.

With a number of patients, however, there is such a special problem in regard to employment, whether it be return to former employment on modified terms or finding a new job, or the taking up of an entirely new occupation. In regard to these cases presenting this problem of reorientation of life and of re-employment, I would like to make the following six suggestions:

(1) The approach to each case must be the individual approach. This is not a matter which can be handled by any mass tactics, or failure is certain. Each patient must be an individual study and must be constantly guided and helped till a satisfactory resettlement has been achieved.

(2) It is essential to be thoroughly well acquainted with the home background in relation to family circumstances, domestic relationships and financial position. It is only by thorough acquaintance with this side of the patient's life that one will be able to prevent an attempt to return to work at too early a date in the course of recovery. Also it is only by close study of all the factors involved that some of the personal and family problems of the patient can be solved.

(3) Direct approach to industry: This is a particularly useful move when we are concerned with re-employment of a patient in the case of whom it is desirable that the return to work should be modified, so that to begin with the day is not too long or too heavy. One has been struck in this connexion by the generous and sympathetic attitude of employers in industry or of personnel managers in large concerns. They are ready to be helpful and there is no question that they are interested and stimulated by personal approach through the almoning services. Better still, as a means of arousing interest, is a visit or a letter from a medical officer concerned with the patient's welfare and future employment.

(4) Ministry of Labour and National Service: The D.R.O.—Disabled Resettlement Officer from local Ministry of Labour Office—is available to interview patients in hospital to help in obtaining employment, and to arrange training for those who require to take up a new occupation. They too are able to provide information regarding the Disabled Persons Employment Act and the register of Disabled Persons. The best use will be made of its possibilities if the almoner and surgeon in charge of the case can unite in presenting to the Ministry of Labour official a picture of what the patient is able to do in the way of work, and a picture of the sociological circumstances.

(5) Voluntary agencies: It is desirable that all concerned with the welfare of problem patients should be familiar with the various voluntary agencies—and they are many—from which assistance can be invoked to meet particular difficulties. Almost invariably one or other of these voluntary agencies will be found invaluable in filling in gaps not covered by the usual official means.

(6) Follow-up: It is very important that the follow-up of ex-patients should be close and intensive, and it is very important that it should have that personal quality referred to as essential in (1). The follow-up is of supreme importance in making sure not only that the patient has obtained employment, but also that the work is within his capacity and suited to the nature of the disability. Apart from this quite obvious usefulness for the individual patient, it is of greatest value in building up our own knowledge and experience. Only by adequate follow-up and study of its findings can we learn how to obviate or to surmount difficulties.

In conclusion, let me refer again to the Disabled Persons Employment Act. This is one of the most revolutionary pieces of social legislation ever introduced, and I doubt if its far-reaching implications are quite properly understood. It will probably take about ten years before we find that the Act is properly worked so that it is the useful piece of legislation that I am sure it is destined to become. The Ministry of Labour will then indeed be worthy of the second part of their official designation which describes them as Ministry of National Service.

As medical men we must do our best to help in the development and the working of the Act, and here we have no small contribution to make to its success. There is another aspect of this Act which has an interest for physicians and surgeons. If properly used it should provide the ideal follow-up, the follow-up which will give us exact information as to the functional usefulness of our patients.

I have referred to this Act as a revolutionary measure. It is indeed outstanding in this regard among the many revolutionary happenings of recent years. I would suggest that we as a profession must also be ready to change. An essayist in the eighties of the last century, referring to men and classes of men who stood out from among their fellows, singled out the medical man as a member of a professional class almost always outstanding. I doubt if a writer on this theme would be justified in saying the same to-day. There is little doubt that as a profession we do not hold the place in the life of the community which we held at the end of the last century. If we are to regain our place as a profession in the community, then I am sure that we must be ready to leave our consulting-rooms and operating theatres and make our way to the market-place, that we must be ready to make friends with industry and that we must adapt our attitude as a profession to a rapidly changing age.

[*February* 12, 1947]

At a Clinical Meeting held at the London Hospital, E.1, the following cases were shown:

(1) **Palindromic Rheumatism.** (2) **Psoriatic Arthritis.**—Dr. W. S. Tegner.

Sclerosis of Left Sacro-iliac Joint.—Dr. R. G. Miller.

Injured Ulnar Nerve (Cat Bite of Right Wrist).—Dr. H. G. Whitworth.

(1) **Bilateral Brachial Neuralgia;** with Osteo-arthritic Changes of C.6 and C.7 (Female). (2) **Left Brachial Neuralgia;** with Osteo-arthritic Changes of C.6 and C.7 (male). (3) **Left Brachial Neuralgia Following a Fall;** X-ray Showed Diminished Disc Space Between C.5 and C.6 (Male).—Dr. K. N. Lloyd.

(1) **Spontaneous Forward Subluxation of Atlas on Axis.** (2) **? Rheumatoid Arthritis and Ankylosing Spondylitis.** (3) **Complete Rupture of Right Quadriceps and Partial Rupture of Left Quadriceps Tendons.**—Mr. R. A. King.

[*March* 12, 1947]

Analysis of Function

By H. Ernest Griffiths, C.B.E., M.S., F.R.C.S.

The selection of the man for the job and the job for the man is a problem which only in the last fifty years has begun to emerge as an exact science.

The industrial psychologist and the time and motion engineer began to develop their technique in a world where man-power was plentiful and labour relatively cheap and when, therefore, the physically disabled were at a discount. It very early became apparent to these research students that success and failure at work resolved themselves into questions of dexterity, temperament and fatigability—or, as the foreman would put it, clumsiness, carelessness and laziness.

Now, in the good old days, before honest toil was complicated by labour managers, psychologists, motion teams and whatnot, the foreman—that rugged child of Nature—hired and fired to the measure of his own yardstick. There was a time (I had almost quoted Goldsmith) before the Industrial Revolution cursed the community with repetitive movement, when production was in the hands of craftsmen working with simple tools but with a skill that had been acquired during long years of apprenticeship. The craftsman was a man of many parts, skilled not only in one aspect of the job, but in the whole trade, and therefore able to devise ways and means to surmount difficulties as they arose. Time and training were both on his side and the many-sidedness of his craft permitted a physical adaptability which might not be possible in the stereotyped jobs so common in modern industry. With the development of the machine tool complicated jobs were broken down into a series of simple operations and craftsmen gave place to teams of semi-skilled machine operators and assemblers.

The development of specialists in relatively simple jobs coupled with the greed for speed, focused a spotlight on those defects in the human mental make-up which meant all the difference between success and failure—dexterity, temperament and fatigability.

The foreman's method of selection by trial and error took no account of the facts that man-power was plentiful, whereas machines were precious and time was golden; industry just could not afford to train unsuitable persons for a technique which they could never master or, worse, risk delay in an operation or damage to a precious machine, possibly to be clogged up with a human limb.

It became imperative, therefore, that methods should be devised for pre-selection of units from the mass of available human material capable of giving the maximum of production with the minimum of waste. And so arose the industrial psychologist, and his opposite number the time and motion engineer, with selection tests, therbligs, process charts, and many other devices. These twin sciences have already to their credit immense achievements not only in the speeding up of production, but in improving working conditions and in devising ways and means of accident prevention.

But in no field of research has obscurity of a forest by trees been more pronounced. Just as the whole of logic is founded on the assumption "I am", so industrial psychology and motion engineering have been built on the assumption of the able-bodiedness of man. This acceptance of the universality of able-bodiedness did not, of course, imply that all men were equal or that there were not great variations in physique.

Able-bodiedness is a matter of physical function, not of shape, size or stature, and physical functional analysis is the determination of the coefficient of able-bodiedness, but physical function is the expression of thought through muscular action. It follows, therefore, that a complete analysis of physical function in any human being would be as impossible of achievement as the tale of his every thought. A practical analysis must, therefore, be attempted within certain limits. When I first used the phrase "Physical functional analysis" many years ago I was concerned solely with the fitting of the disabled into industry and was attempting to assess only those functions which would be in common use in industrial processes. Obviously I had to go to industry before coming back to man and I started to compile an elaborate list of functions which were performed at work such as, reaching, striking, carrying, screw-driving, &c., a study of these functions showed that many of them were composite and could be resolved—thus, screw-driving as generally understood, became grasping, pushing, turning. Finally, a comparatively short list of ordinary functions in industry was compiled and not all of these needed to be split into their ultimate components, e.g. cutting with scissors, humping, striking.

Let us examine "striking" a little further: a simple analysis of the physical effort made in striking with a hammer would show that the hammer is first pushed upwards against gravity and then pulled down so that the act of striking is resolved into pushing and pulling (remember the instruction you have had from your golf professional—pull with the left arm).

Some physical analyses, I think perhaps the majority, are content to leave out striking, holding it covered by its components, pushing and pulling. This is an error which can only be accounted for by the assumption of able-bodiedness. The average man can push a truck and pull a rope and push and pull a hammer, but consider the man with the old ununited fracture of the scaphoid, such a man can push a truck and pull a rope but he cannot push and pull a hammer. . . . Why? First, the obvious answer is that in striking he jars his wrist causing movement between the fragments of the scaphoid or disturbance in the surrounding soft parts. But an analysis of the three functions will show that in pushing a truck, as in pulling a rope, the wrist and carpal joints are held fixed by muscular action throughout the whole operation, whereas in striking with the hammer the wrist only becomes fixed at the moment of impact when the grasp tightens. Striking, therefore, is something more than the two simple acts of push and pull; there is a regular sequence of efforts—push, pull, squeeze—and I use the word "squeeze" here to illustrate increasing the effort of grasp which is itself a constant in all the processes under review. Unless this sudden squeeze is fully appreciated there would be difficulty in explaining the occurrence of tenosynovitis in the forearms of workers whose muscles are not trained to the use of a hammer.

An analysis of physical function is a primary concern of the motion engineer but the analysis considered from a physiological point of view is of an empirical type. Take, for example, the everyday task of polishing a floor: if you are inexperienced in housework—as I was before the war emergency turned me into an expert—perhaps you achieve your object on hands and knees by rubbing back and fore with a polishing rag. But this method would not find favour with the motion engineer (much less your wife): in his analysis he would show that at the commencement of the operation the polishing rag had to overcome inertia and acquire momentum; that the *momentum had to increase to a maximum* and then slow down to a full stop, and that on the reverse stroke inertia again had to be overcome, momentum acquired and quickened and slowed, thus causing loss of time and an immense waste of energy, both in overcoming inertia and in retarding momentum. He would point out that if a circular motion is used instead of a back and fore action most of the lost time and energy is saved, but the motion engineer has assumed able-bodiedness and therefore the ability to change from simple back and fore movement to one of rotation with all its increased problems of joint movement and muscle co-ordination. There is no doubt that experience has shown that the circular motion in hand polishing is much more successful than the back and fore. The first consideration has been the end-result, the polished surface; the time-and-motion study has shown additional reasons in the economy of time and effort.

It is now necessary to study some of the problems of physical effort in polishing with a circular or perhaps somewhat elliptical motion. The industrial psychologist could tell you that the great majority of people when polishing use a motion which is counter-clockwise with the right hand and clockwise with the left hand. Of course there are reasons for this and here are two of them: the flexors of the arm are stronger than the extensors and the power of pull is greater than that of push; in the act of polishing some of the weight of the body is used to maintain contact between the polishing cloth and the floor. The weight of the body is not evenly distributed throughout the stroke, the maximum is used at the moment of maximum physical effort and if this is also at the time when the polishing hand is nearest the centre of gravity of the body, balance is maintained with the minimum of effort. Now, consider the possibility of polishing with the right hand with a clockwise motion: if the maximum weight is to be distributed near the centre of gravity then the maximum effort must be in the push stroke, admittedly weaker than the pull stroke; or alternatively if the maximum weight is to be taken during the pull stroke, well, then it is distributed outside the centre of gravity. The arguments which I have deduced for right-hand polishing in a counter-clockwise motion are obviously applicable to left-hand polishing with a clockwise motion.

One might say that in polishing a floor the right biceps and pectoral muscles come in for a fair share of the work and that, also, the semicircular canals and postural reflexes are all mixed up in the problem. And so what of the charlady who has had a radical mastectomy or who suffers from Ménière's disease?

In this analysis of the effort produced in polishing although we started with the consideration of pull and push, we have been led to the consideration of the effort of maintaining balance. Balance is the ultimate triumph of the postural reflex and needs the functions of the organs of balance or possibly the alternative functions of sight, touch or hearing, plus the integrity of a complicated reflex arc and finally the muscle power to maintain the required position.

The able-bodied person can naturally maintain his balance without effort or thought in normal industrial processes; without conscious effort because as has already been stated, balance is the result of postural reflexes built up of joint sense, the stretch reflex, tonus and other things which are entirely subconscious; but a physical functional analysis of a disabled person may bring to light some physical defect which throws this complicated system out of gear; his employment, therefore, in industry is jeopardized.

Concussion is fairly common amongst dock workers but there are few jobs on the wharf that come strictly within the definition of light work; amongst them, however, is that of banks-man who signals to the crane or winch driver to direct him in the placing of a load. Such a job might be ideal for a man who suffered headache and was better in the open air than indoors. But before placing him it would be better to know whether looking up made him liable to lose his balance and fall in the dock.

I have been trying by simple examples to show the need for physical functional analysis in the placing of the disabled person and that this analysis must play a big part in the future in the work of the industrial psychologist and the motion engineer.

Physical functional analysis is concerned not with the method of performance but with the physical requirements that are necessary to carry out that method or an alternative method calculated to produce the same result. If one is concerned solely with the first part of the definition, namely the carrying out of a particular method, and not the consideration of alternative methods, then it may be possible to consider a limited functional physical analysis as applied to definite anatomical regions of the body; but if alternative methods are to be considered then the function of the body as a whole must be the subject of study. Again, a very clear distinction must be made between physical function and mental function. Take, for example, writing: the action of holding and propelling a pen across paper is entirely physical but the ability to control the pen so that it forms letters is a mental process and once the power to write has been acquired the writing skill is not lost because the usual means of applying that skill are lost, any more than would be the skill to read. If a man learns to read by sight and then becomes blinded he has not lost the power but only the means to read; alternative means can be provided through touch and when he is taught Braille he is only taught to apply a new means to a skill he already possesses.

After a physical function has been defined the analysis must take note of the quality of that function, and here again the distinction between mental and physical function may be difficult to define and in some respects they may be shown to be reversed in the disabled as compared with the able-bodied. As an example, fatigability in the able-bodied is primarily a psychological problem, the degree of bodily fatigue in a process is directly proportionate to the psychological effort involved but this is not necessarily true where the balance of opposing muscles has been upset by disease or possibly injury. Take, for example, the poliomyelitis case with weakness of the leg muscles, or the man with internal derangement of the knee and wasting of the vastus internus muscle: in this latter case the power of sustained tonus may be diminished to such an extent that the knee is apt to give way and balance and security are affected.

Attempts have been made to subdivide physical function into certain constituent parts. McBride suggested quickness, co-ordination, strength, security, endurance, safety, physique—by physique he meant outward appearance, holding that deformity might have an adverse effect upon the morale of the man as well as on the chances of his employment. He has endeavoured to estimate percentage loss of each one of these components and so to arrive at a percentage loss of function as a basis for compensation for industrial injuries. Kessler and others have criticized his methods and have pointed out the many fallacies that must creep in.

Able-bodiedness is a matter of physical function, not of shape, size or stature, and physical functional analysis is the determination of the coefficient of able-bodiedness, but physical function is the expression of thought through muscular action. It follows, therefore, that a complete analysis of physical function in any human being would be as impossible of achievement as the tale of his every thought. A practical analysis must, therefore, be attempted within certain limits. When I first used the phrase "Physical functional analysis" many years ago I was concerned solely with the fitting of the disabled into industry and was attempting to assess only those functions which would be in common use in industrial processes. Obviously I had to go to industry before coming back to man and I started to compile an elaborate list of functions which were performed at work such as, reaching, striking, carrying, screw-driving, &c., a study of these functions showed that many of them were composite and could be resolved—thus, screw-driving as generally understood, became grasping, pushing, turning. Finally, a comparatively short list of ordinary functions in industry was compiled and not all of these needed to be split into their ultimate components, e.g. cutting with scissors, humping, striking.

Let us examine "striking" a little further: a simple analysis of the physical effort made in striking with a hammer would show that the hammer is first pushed upwards against gravity and then pulled down so that the act of striking is resolved into pushing and pulling (remember the instruction you have had from your golf professional—pull with the left arm).

Some physical analyses, I think perhaps the majority, are content to leave out striking, holding it covered by its components, pushing and pulling. This is an error which can only be accounted for by the assumption of able-bodiedness. The average man can push a truck and pull a rope and push and pull a hammer, but consider the man with the old ununited fracture of the scaphoid, such a man can push a truck and pull a rope but he cannot push and pull a hammer. . . . Why? First, the obvious answer is that in striking he jars his wrist causing movement between the fragments of the scaphoid or disturbance in the surrounding soft parts. But an analysis of the three functions will show that in pushing a truck, as in pulling a rope, the wrist and carpal joints are held fixed by muscular action throughout the whole operation, whereas in striking with the hammer the wrist only becomes fixed at the moment of impact when the grasp tightens. Striking, therefore, is something more than the two simple acts of push and pull; there is a regular sequence of efforts—push, pull, squeeze—and I use the word "squeeze" here to illustrate increasing the effort of grasp which is itself a constant in all the processes under review. Unless this sudden squeeze is fully appreciated there would be difficulty in explaining the occurrence of tenosynovitis in the forearms of workers whose muscles are not trained to the use of a hammer.

An analysis of physical function is a primary concern of the motion engineer but the analysis considered from a physiological point of view is of an empirical type. Take, for example, the everyday task of polishing a floor: if you are inexperienced in housework—as I was before the war emergency turned me into an expert—perhaps you achieve your object on hands and knees by rubbing back and fore with a polishing rag. But this method would not find favour with the motion engineer (much less your wife): in his analysis he would show that at the commencement of the operation the polishing rag had to overcome inertia and acquire momentum; that the momentum had to increase to a maximum and then slow down to a full stop, and that on the reverse stroke inertia again had to be overcome, momentum acquired and quickened and slowed, thus causing loss of time and an immense waste of energy, both in overcoming inertia and in retarding momentum. He would point out that if a circular motion is used instead of a back and fore action most of the lost time and energy is saved, but the motion engineer has assumed able-bodiedness and therefore the ability to change from simple back and fore movement to one of rotation with all its increased problems of joint movement and muscle co-ordination. There is no doubt that experience has shown that the circular motion in hand polishing is much more successful than the back and fore. The first consideration has been the end-result, the polished surface; the time-and-motion study has shown additional reasons in the economy of time and effort.

It is now necessary to study some of the problems of physical effort in polishing with a circular or perhaps somewhat elliptical motion. The industrial psychologist could tell you that the great majority of people when polishing use a motion which is counter-clockwise with the right hand and clockwise with the left hand. Of course there are reasons for this and here are two of them: the flexors of the arm are stronger than the extensors and the power of pull is greater than that of push; in the act of polishing some of the weight of the body is used to maintain contact between the polishing cloth and the floor. The weight of the body is not evenly distributed throughout the stroke, the maximum is used at the moment of maximum physical effort and if this is also at the time when the polishing hand is nearest the centre of gravity of the body, balance is maintained with the minimum of effort. Now, consider the possibility of polishing with the right hand with a clockwise

The pure scientist may wish to see each one of these composite functions split up into its ultimate anatomical, physiological, and psychological components; he will want to discuss postural reflexes, conditioned stimuli and so on; and it is all a fascinating and useful study which has an important bearing on methods of medical and surgical treatment, on investigations of conditions and ways of employment, and of the cause and the prevention of accidents. I have referred to some of these problems elsewhere (Hunterian Lecture, "Treatment of the Injured Workman", *Lancet*, 1943 (i), 729) but I am limiting this analysis to a point at which I feel that the expert's analysis will be intelligible to the layman and, therefore, usable by one whose business it is to select the man for the job. In this sense, therefore, the following list may be regarded as one of primary functions:

> Balancing, running, jumping, climbing, kneeling, stooping, crouching, reaching, throwing, lifting, pulling, pushing, striking, carrying, humping, handling, fingering, cutting with scissors, feeling.

You may also think that turning should be added as something distinct from handling and possibly you may wish to include other actions.

Feeling is dependent upon the sense of touch and, of course, no analysis that does not include an intelligible note on the other special senses can be complete, e.g. sight. In general employment it is sufficient to know whether a man can see reasonably well at a distance and whether he can see reasonably small print and also perhaps whether it is necessary for him to wear glasses. It is true that in certain special industries good colour vision is necessary and in some very acute sight; in such industries sight selection tests are necessary and as these cannot be carried out satisfactorily by the ordinary general practitioner, I have not thought it necessary to include them in this primary functional analysis. Similarly, specific tests for hearing and smell and taste are not included.

The human stresses and strains from industrial effort vary enormously with the circumstances in which the effort is made. Let us go back to the sack of potatoes. Supposing the sack is in the middle of a large field; the workman will be exposed to the vagaries of the weather and this may not suit his rheumatism, his bronchitis, or his thrombo-angiitis obliterans. The situation is perhaps so isolated and open as not to be borne by the man with agoraphobia. But perhaps the potatoes are stored in a warehouse. As the sacks are moved the air soon becomes thick with dust to the discomfiture of the chronic asthmatic or the man with ectropion. And so in addition to the place of work the conditions of work become important—dust or damp, extremes of heat or cold, &c.

Certain jobs are fraught with special risks—the window cleaner may fall from a height, the tar sprayer develop cancer of the skin, or the radiographer an aplastic anæmia and so on. Every able-bodied person doing a job is exposed to the risk appertaining to that job but a physical examination of a particular individual may disclose a morbid condition which increases the normal risk. A minor degree of instability in the knee-joint may permit the man to run, climb and jump, and yet it may be just sufficient to interfere with the maintenance of balance on a narrow ledge, which is essential to the safety of a window cleaner.

Thus, the physical functional analysis, whilst listing the possession of certain faculties used in the normal course of industry, would be failing in its purpose of demonstrating employability unless it also qualified its list by indicating any adverse factors in the bodily or mental make-up of the workman which would render him unsuitable for employment in circumstances of exceptional environmental conditions.

Physical functional analysis should be presented as an exact piece of work with the very minimum of medical opinion and the maximum of physiological fact. It should not be attempted unless the physician is prepared to make a thorough routine examination of his patient. As we are dealing now with the practical problem of fitting the able-bodied and the disabled into industry this routine examination must be understood as one that can be undertaken by a painstaking general practitioner or industrial medical officer. I know there are exceptional cases in which the opinion of a specialist may be needed but these *are* exceptions.

After the examination comes the recording of the analysis and this *may* be done as a medical report. Suppose it reads: "This man had a Pott's fracture and is now fit for light work". This would not convey much of your expert knowledge of the man's condition to the layman. The purpose of the physical functional analysis is the selection of the man for the job and this is a task for industry, not medicine. Your analysis, which is a purely medical affair, is of primary importance, but it is not the only important factor in placing the man in work. Do not forget the industrial psychologist and his selection tests, or the labour manager, or the manager of the machine shop—this latter would not have reached his position unless he was something of a psychologist; it may be his opinion that the girls

Perhaps the chief fallacy of this method is that it focuses attention upon local physiological action rather than the result of that action. The estimate of function is not measured in the angle through which a joint can be flexed but in the power of purposeful effort that may be achieved through this action. This power of purposeful action depends upon so many factors beside the flexion of the individual joint that in considering it the investigator is invariably forced back to the consideration of the body as a whole.

The scale, as well as the tale, of human physical function will vary enormously in different individuals. In a particular group all may be able to lift but whereas one can lift 10 lb., another 20 lb. and another 100 lb., the ability to do a particular job may depend on the power to lift 50 lb. or more; thus, the functional analysis recording the ability to lift without some indication of the power is of little value. Suppose the job to be one of lifting sacks of potatoes weighing ½ cwt. 4 ft. from the ground to the back of a lorry; this, of course, is not simply a question of strong arms. Consider how the job is done: the workman lowers his arms to grasp the sack, by the simple expedient of bending his knees and hips—the expert hardly flexes the spine at all—the lift is initiated by extension of the knee-joints and the hip-joints and is then assisted by simultaneous flexion of the elbow-joints and abduction of the shoulders (for the sake of simplicity I am omitting reference to the movement of other joints, such as the mid-tarsals). Given, therefore, a physique with sufficient power in the muscles which control these joints, the workman is capable of doing the work in question—but that is only on the assumption of able-bodiedness. Suppose now that this powerful fellow has a diseased heart: he might have the physical power to perform the task but not the recuperative power to withstand the consequences; such a man is unfit for the work in question and yet his unfitness has not been disclosed by the movement of lifting as we have considered it so far. We must carry the study a little further and consider the trunk in relation to the limbs. At the moment of initiation of the lift and generally throughout the lift, respiration is inhibited: the primary reason for this is to fix the ribs and therefore give points of fixed attachments for the muscles controlling shoulder movement. You will remember that only man and his kind and the cat and her kind have this capacity and therefore they are the only animals that can strike an effective blow from the shoulder. Holding the breath for a moment or two may have no great effect on the ordinary man, but consider one suffering from chronic emphysema—you can see his face getting blue with every effort and before long he has to interrupt his lifting to rest because he cannot compensate for holding his breath by taking a few deep breaths. He is therefore not fit for the job because he has no power of endurance in that particular form of work. This man might have been employed on equally arduous work humping the sacks from the lorry to the store because the action of humping demands regular breathing. Our study has disclosed so far why the ribs are fixed and the breath is held but not how it is done. I need hardly remind you that amongst other happenings there is contraction of the diaphragm and of the great muscles of the abdominal wall, including the rectus, external and internal obliques, transversalis and quadratus lumborum. The first three of these are flexors of the spine; any attempt at faulty lifting by using the erector spinæ muscles to extend a flexed spine will be against the resistance of these flexors and therefore inviting a "strained back". This is an important consideration in giving a man with a stiff knee a job involving lifting from the ground level.

But there is another consequence of fixing the lower ribs. As the diaphragm is forced down and the other muscles of the abdominal wall contract, the pressure within the abdominal cavity rises and any tendency to hernia may be exposed.

We have made a superficial study of the behaviour of the limbs, trunk, heart and lungs during the act of lifting a 56 lb. sack, but have not considered the mechanics of the whole movement. I will only draw attention to the subject of balance without which the whole effort fails.

It should now be apparent that in making a physical functional analysis as a means of determining employability or capacity for particular work, there are certain considerations of the general bodily state which must take precedence over the determination of the ability to perform certain specific evolutions.

First comes stamina: has the man the power of physical endurance necessary to work through the hours that are expected of him—the hardest man to place in industry is the man who can only work broken time. Next to this comes the estimation of power, the ability to withstand the required physical strain, say, one equivalent to the lifting of a 56 lb. weight. Then comes balance or the ability to maintain the body in the required positions.

Only when the general bodily state has been determined can we move on to the delineation of other faculties. At the outset of this more detailed study we must resign ourselves to the acceptance of certain complicated movements as though they were not capable of being resolved into simpler actions; e.g. running, jumping, climbing.

was opened. I was told that as a surgeon I was not capable of recognizing neurosis. My reply was that perhaps there might have been a patient in whom I had not noticed the neurosis but my patient did not notice it either, and he had gone back to work and his employer had not noticed it, and at the end of the week he had taken home a full pay packet and his wife had not noticed it; and so what the . . . ! But nevertheless there are certain obvious and important defects which may be grouped under "nervous state" and which will affect employability, e.g. stammer, tremor and fits.

Normally vision for the purposes of ordinary work implies the ability to see at a distance and to perform reasonably fine work as in reading ordinary newspaper print. The loss of sight in one eye, provided the other eye be normal, has very little effect upon employability except in certain occupations where standards of physical health are laid down as conditions of employment. The routine examination is quite sufficient to fill in the section on vision as it is for the section on hearing.

On page 6-G three sections are devoted to environment including place of work, working conditions and special hazards. Almost each one of the special conditions recorded has some disadvantage for the able-bodied person. Therefore they only need comment if such conditions would cause special hardship to the individual concerned, e.g. the gastric case may be at a disadvantage if there is no canteen at his place of work where he can get reasonable food or if he has to engage in shift work and so upset the routine of normal feeding. The information under this heading of environment is of great importance to the D.R.O. and it is precisely this information that is omitted in the great majority of written medical reports.

What may be termed the true analysis of function ends on page 6 but on page 7 there is a short form of medical certificate dealing with prognosis and treatment. In this connexion H-3 has already been answered.

I hope that by now I have convinced you that if it falls to your lot to submit to the D.R.O. an opinion on the capacity for work of one of your patients the easiest, quickest and most comprehensive method of doing so will be by filling in this report form—a task which should take you well under three minutes.

The major use to which a functional analysis can be put in the employment of the disabled person is in determining those limits within which he may perform ordinary work by the ordinary methods. A second important use is in supplying information for the selection of alternative methods in performing ordinary work, e.g. driving a screw into a hole in wood. If the workman is watched carefully it will be seen that: (*a*) he reaches out with his left hand and selects a screw from a container, often without looking; (*b*) he picks up the screwdriver with the right hand; (*c*) places the screw in position with the left hand, looks at the head of the screw and places the screwdriver in position; (*d*) with his eye on the screw he exerts pressure through the screwdriver and at the same time rotates the driver in a clockwise direction.

All these might have been expressed in terms of functional analysis as: (*a*) reaching, feeling, fingering; (*b*) handling, lifting; (*c*) seeing, handling; (*d*) seeing, pushing, handling (or turning).

Now the first analysis with its reference to right and left hands and to the eyes suggests that the work of driving a screw into a hole is necessarily a two-handed job for a man with good eyesight. The second analysis only details function and makes no reference to the means of its performance. Reaching, feeling, fingering, handling, lifting, seeing, pushing, turning; with these functions grouped together thus it becomes apparent at once that here is scope for the employment of substitute functions. Take, for example, feeling and seeing; these are complementary to each other; the blind man can drive in a screw perfectly well because he uses feeling instead of his sight, and the man who has lost the sensory nerve to the fingers can select and pick up a screw if he looks at it. This work may be done by a blind man or a man who has lost the feeling in his fingers; it may be done by a one-armed man or even the man with no arms if fitted with suitable appliances and if able to see.

Perhaps I have already said enough to show how great a difference there is between the analysis of function and a purely physical examination and also to show how the one can never be matched with the other. Physical examination means the regional study of the body, whereas functional analysis must mean the study of the body as a whole. It is for this reason that these schedules of disabilities that are so constantly used as methods of assessment in pensions schemes fail so completely when used to indicate how much the individual has lost or how much he falls below able-bodiedness as the result of his scheduled disability. The schedule is a scale of physical disability; an analysis of function is the study of the man.

on a particular machine won't keep their minds on the job if the new tool-setter, however capable, is a red-head.

Much of the value of your analysis will depend on the way in which it is set out and therefore on the way in which it makes available and intelligible to the lay mind the result of your research—and each medical examination you make is an important piece of research. An outline for a medical report in the form of a functional analysis, the D.P.1, is issued by the Ministry of Labour and National Service and is intended to help the medical examiner to furnish all the medical data which the D.R.O. may require before recommending a disabled person for employment in a particular industry.[1] This form was the product of the labour of the Hooper Committee, a joint committee set up by the Ministries of Labour, Health and Pensions. It is not claimed that the form is perfect, experience in its use may result in minor or important modifications; or it may be scrapped. Experience has already shown that whereas the ordinary written report of a doctor may enable the D.R.O. to decide whether a man is suitable for registration as a disabled person, it is quite valueless as a guide to his employability.

This form at first sight appears to be not only complicated, but alarming; but if it is once read through, which may take you five whole minutes, I think it will be appreciated that it is really a great time- and labour-saving device. It does nothing to shorten the medical examination. As I have already stated the thoroughness of the medical examination is the first essential of any functional analysis: but when the examination has been made it saves both time in writing and thought in composition. Finally, it is almost certain to obviate many sins of omission.

The doctor's share in the filling of the D.P.1 starts on page 2 with the diagnosis and, if he knows it, the M.R.C. Code No. This page is unessential for the prime purpose of the report but is useful for research and follow-up.

Page 3 is a functional analysis of the individual as a whole given in the broadest sense and enables the D.R.O. to make his preliminary classification. The whole page can be filled up in five seconds by making five ticks, provided there are no special circumstances requiring a short note in paragraph 2. In practice paragraph 2 on this page does not need filling up in 1% of the cases. Now the five ticks you have placed will have drawn for the D.R.O. a picture something like this. Here is a man who is capable of working a 44-hour week (full time) provided that his place of work is within a mile of his home (restricted travelling) and that he is not called upon to exert a physical strain that is greater than one which would be imposed upon him by the lifting of a 56 lb. weight (medium). He is capable of doing work that involves walking about but he can only work indoors. If you had been writing the report I wonder if you would have thought it necessary to give all this information and, if you had, whether you could have done it in five seconds; and yet it has enabled the D.R.O. to decide in his mind that this man must almost certainly be found employment in a factory, shop or office, and all those fields of labour like agriculture, coal-mining, shipping and transport are closed to him.

Turn now to page 4. The majority of people who are examined will possess the majority of the functions recorded on this page and therefore it is only necessary to indicate those that are lost by placing a cross in the appropriate column. Your examination will have given you the information that should be necessary to decide if a cross is indicated but if there is any doubt the easiest way of finding out is by simple trial. There may be one or two of these functions of which you are not quite certain; perhaps humping, handling and fingering may need a little explaining and they are defined upon the next page. Humping is a technical term used throughout industry for carrying a load on the back; it does not involve lifting the load into position on the back. Handling is a word used to cover those functions in the hand that do not necessarily require special dexterity, such as holding, grasping and turning. You will note that no mention is made of loss of part or all of fingers; a hand may have some mutilation and still retain good power of handling. Fingering, on the other hand, implies the dexterous use of individual fingers as in the pincer grip between the thumb and the index finger or in the use of a needle or a typewriter. Unless the examiner feels that some special comment should be made on any one of the above, this page can be filled in a few seconds.

Page 5 records the nervous state and the vision. The estimation of the nervous state is arrived at during the routine examination and does not imply or require a special psychiatric examination. I remember some time ago being very severely taken to task by a psychiatrist because I said that not a single case of neurosis had occurred in my Fracture Clinic since it

---

[1] A copy of Form D.P.1 accompanies this issue of the "Proceedings".

Section of Psychiatry

President—Professor AUBREY LEWIS, M.D.

[*January* 14, 1947]

The Morphological Level of Personality

By J. M. TANNER, M.B., D.P.M.Lond., M.D.Penn.

(*Anthropological Laboratory, Dept. of Human Anatomy, Oxford University*)

(1) THE CLASSIFICATION OF PHYSIQUE

AT the present time there are, I think, only two classifications of physique that need to be considered at length. Both these systems, as well as the one previously widely used but now obsolete, were devised by psychologists, in a sphere where one might have thought anatomists and physical anthropologists would naturally have dominated research. The first system—I do not mean to imply the first in time, because both were devised contemporaneously and independently over a number of years—the first is that of William Sheldon, published in 1940, now generally quite well known and by virtue of a later publication on temperament, something of a storm centre [1, 2]. The second is that of Sir Cyril Burt, and arose from the application to measurements of the body of the statistical technique of factor analysis, which he has been so prominent in developing as applied to mental tests [3]. A somewhat similar technique has been developed by Professor Mahalanobis of Calcutta, and is now being applied for the first time to problems of physique, in India [4]. In the United States also the factor analysis technique has been used for studying body build, most notably by Carter and Krause in California, McCloy at Iowa, and by Mullen, under the guidance of Prof. Karl Holzinger, in Chicago [36 to 39]. Though these studies have not developed as far or as clearly as have Burt's, the earliest of them preceded Burt's initial publication [35]; they have all been reported, however, in journals of very restricted circulation in this country, and have not been previously remarked here.

I have already implied that the classification of Kretschmer, which consolidated many major advances at the time of its publication, is now obsolete. This is because Sheldon's system has all the advantages of Kretschmer's, and only some of its disadvantages, besides differing from it in a very important and fundamental way. Kretschmer's fundamental mistake was the division of mankind into disparate *types*. He assumed the existence of a trimodal distribution, with large numbers of people belonging to each of his types, and some as mixtures. He failed to grasp the idea of continuously varying *components* of body build, each distributed smoothly and unimodally in the population. Sheldon began from the premise of continuous components; he writes: "The concept of types has been useful in the study of personality, but, like the poles supporting a clothes-line, it provides only end suspension for distributive classifications. As the line becomes filled, the notion of types recedes and finally vanishes altogether, perhaps submerged under a smooth distribution. The path of progress is from the notion of dichotomies to the concept of variation along dimensional axes" [1].

Sheldon began by sorting nude standardized photographs, showing front, side and back views, of 4,000 college students. Disregarding the attribute of largeness or size, he found three extremes of body build present, representing the ends of the distributions, then, of three components. Every individual had now to be assigned a place in the distribution of each component; everyone had *some* of each component in his make-up. Using a 7 point, equal-appearing interval scale, Sheldon rated each individual on each component. Thus the first extreme example was rated as 7–1–1, scoring 7, the maximum, in the first component, and 1, the minimum, in the other two. The second was 1–7–1, and the third 1–1–7. The three components were named endomorphy, mesomorphy and ectomorphy.

Dr. Frank Howitt congratulated Mr. Griffiths on his Address and said that this was an important contribution to purposeful doctoring. He drew attention to the fact that such an analysis had been in force in the Army during the latter stages of the War under the name of P.U.L.H.E.M.S. This was a functional analysis of the whole man based on the mental and physical capacity of the individual in relation to physique, strength, hearing, eyesight, mental stability, &c. A similar assessment had been made of the requirements of all the 600 odd Army trades, so that it was an easy matter for the Hollerith machine to place recruits into occupations which would appear most fitted to their potential capacities. He wondered whether some simplified form of this successful Army experiment could not be translated into civilian usage with advantage.

He also drew attention to the importance of previous training for any given job. It was unwise to assess a man's capacity for the performance of any work or movement without previously instructing him in the correct methods of its execution. Even simple tasks such as jumping, lifting and climbing are very imperfectly performed by the average individual, owing to ignorance of technique. Assessment of functional capacity should, therefore, be delayed until the opportunity of such instruction has been given.

Mr. R. E. Gomme (Ministry of Labour) said that the Ministry's experience of the form D.P.I was limited because it had not so far been used by hospitals in respect of patients discharged with some residual disability. Such experience as they had of the form was sufficient, however, to indicate its real value to the lay staffs of Employment Exchanges (the D.R.O.s) whose duty it was to advise disabled applicants on the kind of employment best suited to their disability and ability. The form gave the D.R.O. a general picture of the applicant's functional capacity and thus helped him to talk both to the applicant and to prospective employers with a certain amount of confidence. Mr. Gomme said that it was intended to use the form under the new Interviewing Scheme which it was hoped to introduce shortly and which would include an opportunity for discussion between the doctors and the D.R.O. Though there had been some criticism of the form on minor points of detail, it had been welcomed by medical members of Disablement Advisory Committees and their Panels—and so far as the Ministry was aware, by the Medical Profession generally.

Dr. Mark Hewitt (Regional Medical Consultant) began by referring to the words written by Galen in A.D. 172 that "Full employment is essential to human happiness, work is Nature's best physician."

At the moment many hospital doctors were not fully aware of the therapeutic value of work, and although they were concerned about nursing, specific treatment, non-specific treatment, physiotherapy and the like, they did not fully appreciate the important fact that full employment was the be-all and end-all of their treatment, and in view of this they were not at the moment taking full advantage of the facilities being offered for the placement of their patients in industry after treatment in hospital.

Many schemes had been formulated, especially in the United States, for job analyses and job placement. Some of the schemes had involved the drawing-up of various categories of the disabled on the one hand, with large lists of the various types of jobs for disabled on the other, but these mass placement schemes took individual personality very little into account, and would not at the moment seem to be a practical measure. He felt that the time for this type of work had not yet arrived, and placement could only be of an individual nature.

In Manchester they were attempting, in conjunction with Professor Crighton Bramwell of the Manchester Royal Infirmary, a scheme for individual job placement of cardiac patients. The unemployed cardiac patient was fully examined, an accurate diagnosis made and a therapeutic classification given according to the amount of work possible. The various jobs, i.e. the cotton and the engineering industries, were being closely surveyed and assessed for their work requirements. In co-operation with the Almoner, personal factors such as travelling, domestic circumstances, &c., would be taken into consideration, and by this means it was hoped to place this group of cases in the most suitable type of work fitted to their disability, and, more important still, to follow their progress.

The Industrial Medical Officer had an important role to play in seeing that the disabled person was satisfactorily resettled in a suitable job, and the importance could not be over-emphasized of the Industrial Medical Officer, D.R.O. and the hospital doctor working as a team in all matters where unemployed disabled were under consideration.

Section of Psychiatry

President—Professor AUBREY LEWIS, M.D.

[*January* 14, 1947]

The Morphological Level of Personality

By J. M. TANNER, M.B., D.P.M.Lond., M.D.Penn.

(*Anthropological Laboratory, Dept. of Human Anatomy, Oxford University*)

(1) THE CLASSIFICATION OF PHYSIQUE

AT the present time there are, I think, only two classifications of physique that need to be considered at length. Both these systems, as well as the one previously widely used but now obsolete, were devised by psychologists, in a sphere where one might have thought anatomists and physical anthropologists would naturally have dominated research. The first system—I do not mean to imply the first in time, because both were devised contemporaneously and independently over a number of years—the first is that of William Sheldon, published in 1940, now generally quite well known and by virtue of a later publication on temperament, something of a storm centre [1, 2]. The second is that of Sir Cyril Burt, and arose from the application to measurements of the body of the statistical technique of factor analysis, which he has been so prominent in developing as applied to mental tests [3]. A somewhat similar technique has been developed by Professor Mahalanobis of Calcutta, and is now being applied for the first time to problems of physique, in India [4]. In the United States also the factor analysis technique has been used for studying body build, most notably by Carter and Krause in California, McCloy at Iowa, and by Mullen, under the guidance of Prof. Karl Holzinger, in Chicago [36 to 39]. Though these studies have not developed as far or as clearly as have Burt's, the earliest of them preceded Burt's initial publication [35]; they have all been reported, however, in journals of very restricted circulation in this country, and have not been previously remarked here.

I have already implied that the classification of Kretschmer, which consolidated many major advances at the time of its publication, is now obsolete. This is because Sheldon's system has all the advantages of Kretschmer's, and only some of its disadvantages, besides differing from it in a very important and fundamental way. Kretschmer's fundamental mistake was the division of mankind into disparate *types*. He assumed the existence of a trimodal distribution, with large numbers of people belonging to each of his types, and some as mixtures. He failed to grasp the idea of continuously varying *components* of body build, each distributed smoothly and unimodally in the population. Sheldon began from the premise of continuous components; he writes: "The concept of types has been useful in the study of personality, but, like the poles supporting a clothes-line, it provides only end suspension for distributive classifications. As the line becomes filled, the notion of types recedes and finally vanishes altogether, perhaps submerged under a smooth distribution. The path of progress is from the notion of dichotomies to the concept of variation along dimensional axes" [1].

Sheldon began by sorting nude standardized photographs, showing front, side and back views, of 4,000 college students. Disregarding the attribute of largeness or size, he found three extremes of body build present, representing the ends of the distributions, then, of three components. Every individual had now to be assigned a place in the distribution of each component; everyone had *some* of each component in his make-up. Using a 7 point, equal-appearing interval scale, Sheldon rated each individual on each component. Thus the first extreme example was rated as 7–1–1, scoring 7, the maximum, in the first component, and 1, the minimum, in the other two. The second was 1–7–1, and the third 1–1–7. The three components were named endomorphy, mesomorphy and ectomorphy.

Fig. 1[1] shows three individuals fairly near the extremes. The man high in endomorphy and low in mesomorphy and ectomorphy is, speaking in caricature, spherical; a sort of globule with a round head, large fat abdomen which predominates over his thorax, and weak floppy, penguin-like arms and legs. The second is the physical training instructor caricature, with cubical massive head, muscular neck, broad and muscled chest, and thick strong muscular arms and legs. The third, again in caricature, disappears when you look at him sideways; he has a thin peaked face with a receding chin and a high forehead, a thin narrow chest and abdomen, and spindly arms and legs. Naturally, only a very small percentage of people look like this; the majority have a moderate amount of each component, and so have as their *somatotype*, as the set of 3 ratings is called, such numbers as 433, 344 or 352. The number of possible combinations of 7 things taken three at a time is 343, but the three components are not independent. They are negatively correlated, so that a high rating in one precludes to some extent high ratings in the others. Thus 771s and 555s do not exist, but 641s and 444s do. 76 somatotypes occurred in Sheldon's 4,000 pictures, and only 50 were at all common. *It must be clearly emphasized that the somatotype is not like the conception of the old fixed type, however; it merely results from making artificial discontinuities in a continuous scale.* The somatotype is a pigeon-hole into which is placed everybody who, on the continuous scales, is nearer that pigeon-hole than any other. In fact, most workers in this field now use halves on the rating scale, converting it to a thirteen-point scale, with a correspondingly larger number of smaller pigeon-holes.

One secondary point in Sheldon's classification must be mentioned here, because we will return to it at the end of this paper. It concerns the degree to which the male body resembles the female and vice versa. Sheldon calls this attribute the *gynandromorphic component*, and rates his subjects on this, again on a 7-point scale. The amount of femininity of build is not independent of the somatotype entirely, but different members of the same somatotype may nevertheless differ quite considerably in the gynandromorphic component. The man who is high in gynandromorphy has, amongst other features, large hips relative to his shoulders, a protuberance of fat above the symphysis, a fullness in the mammary area, and an approximation or overlap of the thighs when the heels are held together.

Having distinguished his somatotypes subjectively, Sheldon then put them on an anthropometric basis. The somatotype of a given individual may be found, without any element whatsoever of subjectivity, by another worker, who takes the standardized photographs, measures 17 diameters of the body from them, and consults Sheldon's tables. (At least this is theoretically so, but, so far, tables have only been published for the 16 to 20 age-group.) Thus any investigator who takes the trouble to measure his photographs may reach precisely those conclusions which Sheldon would have reached, and his results will be comparable with Sheldon's. However, the *original* scale still remains a subjectively determined one, set up by the operation of judgment of equal-appearing increments of somewhat complex stimuli. The root objection to Sheldon's system springs from this fact, that we do not know much about the nature of such scales. Consequently the further statistical manipulation of somatotype data is hazardous. A secondary, allied objection is that we are limited to making discrete jumps in our ratings across portions of the background scale: we cannot interpolate values from anthropometry with confidence, because of this uncertainty of the scale.

The factor analysis of physique, developed chiefly under the guidance of Sir Cyril Burt [5], meets both these objections. The technique is one of the forms of mathematical analysis designed to reduce to human comprehension large numbers of measurements taken simultaneously of several variables. In Burt's hands, this consists of reducing a matrix of covariances or correlation coefficients, such as may be obtained from a series of measurements on the body, to the result of the linear combination of a few other, mutually independent measures, called factors. Thus if we have three factors, A, B, and C, which together designate body build, we can describe a given individual not as measuring such and such in height, weight, leg length, head circumference, chest depth and so on, but more simply as so much of factor A plus so much of factor B plus so much of factor C. Put thus the method sounds similar to Sheldon's, and, indeed, so it is, in essence. The differences spring from the uncertainty of Sheldon's scale, and more importantly, as we shall see, from the fact that Sheldon's components are correlated, while Burt's factors are not.

We can tackle the first point by way of some of Burt's results. The analysis of his latest and most complete data [6] leads to a general factor, a main bipolar factor, and several other factors we shall discuss later. This first bipolar factor has been called the leptosome-pachysome factor by Burt, because its positive saturations are with girth and its negative with length, notably stature, leg length and arm length. Burt also worked out the multiple regression equation for this factor score, in terms of height, weight and leg length; measurements which, to within a small margin represented by a multiple correlation of 0·96, serve to estimate the factor. He was kind enough to let me have this equation in advance of publication, since I happened to possess these measurements on 50 students who had also been somatotyped anthroposcopically by Dr. C. W. Dupertuis, one of Sheldon's close associates, and myself in 1943. Fig. 2 shows the relation between estimated ectomorphy and Burt's leptosomic factor. It is quite obvious that Sheldon and Burt are measuring the same thing, perhaps in slightly different ways. Furthermore, allowing for some errors in the estimation of ectomorphy (since it was not done anthropometrically), for the fact that I had not taken leg measurements in precisely the same way as Burt's measurer, Dr. Morant, and for Burt's regression equation not being absolutely stable if other original measurements are taken, I suspect that the relationship is a straight linear one. The correlation coefficient is −·94. (There is a curious failure to assign any 3½ ratings and if some of the 4 and 4½ ratings were reduced, as this lack might reasonably indicate they should be, the correspondence to linearity would be still closer.) If this proves on further testing to be the case, then we can say that at least as far as ectomorphy is concerned, Sheldon's scale and Burt's are of a precisely similar nature [7], and that the analogue of the Weber effect did not occur, as Sheldon suggested it might have done, in his ratings [1, page 125]. (The other possibility is that the midrange ratings are somewhat inflated, as Sheldon suggests they may be.)

---

[1] *Owing to the paper shortage it is not possible to publish the figures referred to in this paper. Copies of figs. 2 to 6 can, however, be obtained from the author.*

Now this makes it immediately impossible for any other of Burt's factors to correspond with mesomorphy or endomorphy, since the factors are independent and uncorrelated and the components are not. Could we then represent Sheldon's components by two further *oblique* factors; that is, factors which are themselves correlated? Such would seem to be a possibility, at least. But a further question, I think, must arise here, and that the simple one, why bother? Is there any advantage of oblique over orthogonal factors, or any disadvantage? This is ground fought over to exhaustion by the various schools of factorists; Thomson perspicaciously remarks that "it is really impossible to decide between them (the alternative procedures) without first deciding why we want to make factorial analyses at all" [8]. This I think we are in a better position to decide, with regard to physical measurements, than the psychologists are with regard to mental ones.

Factorial analysis, like any other statistical procedure, is a method for classifying things (or, speaking more strictly, events). Now classifications depend for their use on their *usefulness*, and the most desirable classification is that which, at the time of its use, sheds most light on the relations between one set of facts and another. We must then decide what sort of classification in the sphere of physique is most useful in illuminating studies of personality. We may interject here a way of considering personality. I wish to consider the word as referring to the sum total of all the attributes of a human organism, attributes which we describe at various *levels*. These levels on which we abstract and describe personality may be roughly defined following the traditional scientific divisions—anatomical, physiological and psychological, with the last divided into levels of temperament, character, disposition, cultural behaviour and so forth. A certain amount of knowledge has now accumulated on each of these levels, but the synthesis as between one level and another still lags behind in its development. If, then, we are primarily concerned with furthering this development, the usefulness of the classification we adopt at any one level depends on whether such a classification will serve to link up our knowledge with knowledge on another level.

How does such a criterion apply to the classifications of factor analysis? The factors derived from factorial analyses, as Burt has insisted, are statistics in exactly the same sense as a standard deviation or a standard error. They cannot be reified, *a priori;* that is the factors cannot be taken to be anything more than principles of classification, cannot *a priori* be equated with physiological or psychological events, the effects of a certain hormone, for example, or a so-called property of the mind. But though factors cannot *a priori* be reified, they *may*, on occasions, represent the direct expression of a physiological or psychological event. Now it seems to me to follow from what we have said that a factor will only prove useful if in fact it *can* be reified. It is here that the physical anthropologist has a great advantage over the psychologist. He has a number of other facts about growth and physiology which can guide him in judging whether a given set of factors can reasonably be reified, and if so, what, physiologically speaking, they represent. The psychologist usually has to rely on his intuitions about the structure of the mind.

Our decision then as between oblique or orthogonal factors, Sheldon's components (better quantitated, perhaps, in the future) or Burt's factors lies in their correlations with other measurements at other levels, above or below their own, of personality. Judged thus, Sheldon's system has already proved its usefulness by its relations to temperament, if, indeed, future work on Sheldon's measures of temperament (and not somebody else's different ones) confirms the relationship. Burt's factors have not up till the present time been securely linked with

Fig. 1[1] shows three individuals fairly near the extremes. The man high in endomorphy and low in mesomorphy and ectomorphy is, speaking in caricature, spherical; a sort of globule with a round head, large fat abdomen which predominates over his thorax, and weak floppy, penguin-like arms and legs. The second is the physical training instructor caricature, with cubical massive head, muscular neck, broad and muscled chest, and thick strong muscular arms and legs. The third, again in caricature, disappears when you look at him sideways; he has a thin peaked face with a receding chin and a high forehead, a thin narrow chest and abdomen, and spindly arms and legs. Naturally, only a very small percentage of people look like this; the majority have a moderate amount of each component, and so have as their *somatotype*, as the set of 3 ratings is called, such numbers as 433, 344 or 352. The number of possible combinations of 7 things taken three at a time is 343, but the three components are not independent. They are negatively correlated, so that a high rating in one precludes to some extent high ratings in the others. Thus 771s and 555s do not exist, but 641s and 444s do. 76 somatotypes occurred in Sheldon's 4,000 pictures, and only 50 were at all common. *It must be clearly emphasized that the somatotype is not like the conception of the old fixed type, however; it merely results from making artificial discontinuities in a continuous scale.* The somatotype is a pigeon-hole into which is placed everybody who, on the continuous scales, is nearer that pigeon-hole than any other. In fact, most workers in this field now use halves on the rating scale, converting it to a thirteen-point scale, with a correspondingly larger number of smaller pigeon-holes.

One secondary point in Sheldon's classification must be mentioned here, because we will return to it at the end of this paper. It concerns the degree to which the male body resembles the female and vice versa. Sheldon calls this attribute the *gynandromorphic component*, and rates his subjects on this, again on a 7-point scale. The amount of femininity of build is not independent of the somatotype entirely, but different members of the same somatotype may nevertheless differ quite considerably in the gynandromorphic component. The man who is high in gynandromorphy has, amongst other features, large hips relative to his shoulders, a protuberance of fat above the symphysis, a fullness in the mammary area, and an approximation or overlap of the thighs when the heels are held together.

Having distinguished his somatotypes subjectively, Sheldon then put them on an anthropometric basis. The somatotype of a given individual may be found, without any element whatsoever of subjectivity, by another worker, who takes the standardized photographs, measures 17 diameters of the body from them, and consults Sheldon's tables. (At least this is theoretically so, but, so far, tables have only been published for the 16 to 20 age-group.) Thus any investigator who takes the trouble to measure his photographs may reach precisely those conclusions which Sheldon would have reached, and his results will be comparable with Sheldon's. However, the *original* scale still remains a subjectively determined one, set up by the operation of judgment of equal-appearing increments of somewhat complex stimuli. The root objection to Sheldon's system springs from this fact, that we do not know much about the nature of such scales. Consequently the further statistical manipulation of somatotype data is hazardous. A secondary, allied objection is that we are limited to making discrete jumps in our ratings across portions of the background scale: we cannot interpolate values from anthropometry with confidence, because of this uncertainty of the scale.

The factor analysis of physique, developed chiefly under the guidance of Sir Cyril Burt [5], meets both these objections. The technique is one of the forms of mathematical analysis designed to reduce to human comprehension large numbers of measurements taken simultaneously of several variables. In Burt's hands, this consists of reducing a matrix of covariances or correlation coefficients, such as may be obtained from a series of measurements on the body, to the result of the linear combination of a few other, mutually independent measures, called factors. Thus if we have three factors, A, B, and C, which together designate body build, we can describe a given individual not as measuring such and such in height, weight, leg length, head circumference, chest depth and so on, but more simply as so much of factor A plus so much of factor B plus so much of factor C. Put thus the method sounds similar to Sheldon's, and, indeed, so it is, in essence. The differences spring from the uncertainty of Sheldon's scale, and more importantly, as we shall see, from the fact that Sheldon's components are correlated, while Burt's factors are not.

We can tackle the first point by way of some of Burt's results. The analysis of his latest and most complete data [6] leads to a general factor, a main bipolar factor, and several other factors we shall discuss later. This first bipolar factor has been called the leptosome-pachysome factor by Burt, because its positive saturations are with girth and its negative with length, notably stature, leg length and arm length. Burt also worked out the multiple

[1] *Owing to the paper shortage it is not possible to publish the figures referred to in this paper. Copies of figs. 2 to 6 can, however, be obtained from the author.*

regression equation for this factor score, in terms of height, weight and leg length; measurements which, to within a small margin represented by a multiple correlation of 0·96, serve to estimate the factor. He was kind enough to let me have this equation in advance of publication, since I happened to possess these measurements on 50 students who had also been somatotyped anthroposcopically by Dr. C. W. Dupertuis, one of Sheldon's close associates, and myself in 1943. Fig. 2 shows the relation between estimated ectomorphy and Burt's leptosomic factor. It is quite obvious that Sheldon and Burt are measuring the same thing, perhaps in slightly different ways. Furthermore, allowing for some errors in the estimation of ectomorphy (since it was not done anthropometrically), for the fact that I had not taken leg measurements in precisely the same way as Burt's measurer, Dr. Morant, and for Burt's regression equation not being absolutely stable if other original measurements are taken, I suspect that the relationship is a straight linear one. The correlation coefficient is −·94. (There is a curious failure to assign any 3½ ratings and if some of the 4 and 4½ ratings were reduced, as this lack might reasonably indicate they should be, the correspondence to linearity would be still closer.) If this proves on further testing to be the case, then we can say that at least as far as ectomorphy is concerned, Sheldon's scale and Burt's are of a precisely similar nature [7], and that the analogue of the Weber effect did not occur, as Sheldon suggested it might have done, in his ratings [1, page 125]. (The other possibility is that the midrange ratings are somewhat inflated, as Sheldon suggests they may be.)

Now this makes it immediately impossible for any other of Burt's factors to correspond with mesomorphy or endomorphy, since the factors are independent and uncorrelated and the components are not. Could we then represent Sheldon's components by two further *oblique* factors; that is, factors which are themselves correlated? Such would seem to be a possibility, at least. But a further question, I think, must arise here, and that the simple one, why bother? Is there any advantage of oblique over orthogonal factors, or any disadvantage? This is ground fought over to exhaustion by the various schools of factorists; Thomson perspicaciously remarks that "it is really impossible to decide between them (the alternative procedures) without first deciding why we want to make factorial analyses at all" [8]. This I think we are in a better position to decide, with regard to physical measurements, than the psychologists are with regard to mental ones.

Factorial analysis, like any other statistical procedure, is a method for classifying things (or, speaking more strictly, events). Now classifications depend for their use on their *usefulness*, and the most desirable classification is that which, at the time of its use, sheds most light on the relations between one set of facts and another. We must then decide what sort of classification in the sphere of physique is most useful in illuminating studies of personality. We may interject here a way of considering personality. I wish to consider the word as referring to the sum total of all the attributes of a human organism, attributes which we describe at various *levels*. These levels on which we abstract and describe personality may be roughly defined following the traditional scientific divisions—anatomical, physiological and psychological, with the last divided into levels of temperament, character, disposition, cultural behaviour and so forth. A certain amount of knowledge has now accumulated on each of these levels, but the synthesis as between one level and another still lags behind in its development. If, then, we are primarily concerned with furthering this development, the usefulness of the classification we adopt at any one level depends on whether such a classification will serve to link up our knowledge with knowledge on another level.

How does such a criterion apply to the classifications of factor analysis? The factors derived from factorial analyses, as Burt has insisted, are statistics in exactly the same sense as a standard deviation or a standard error. They cannot be reified, *a priori;* that is the factors cannot be taken to be anything more than principles of classification, cannot *a priori* be equated with physiological or psychological events, the effects of a certain hormone, for example, or a so-called property of the mind. But though factors cannot *a priori* be reified, they *may*, on occasions, represent the direct expression of a physiological or psychological event. Now it seems to me to follow from what we have said that a factor will only prove useful if in fact it *can* be reified. It is here that the physical anthropologist has a great advantage over the psychologist. He has a number of other facts about growth and physiology which can guide him in judging whether a given set of factors can reasonably be reified, and if so, what, physiologically speaking, they represent. The psychologist usually has to rely on his intuitions about the structure of the mind.

Our decision then as between oblique or orthogonal factors, Sheldon's components (better quantitated, perhaps, in the future) or Burt's factors lies in their correlations with other measurements at other levels, above or below their own, of personality. Judged thus, Sheldon's system has already proved its usefulness by its relations to temperament, if, indeed, future work on Sheldon's measures of temperament (and not somebody else's different ones) confirms the relationship. Burt's factors have not up till the present time been securely linked with any physiological or psychological correlates. Later in this paper we shall, therefore, be concerned with establishing the relations of these factors to events during the growth of the child.

(2) Physiology, Growth and Physique

I have the feeling that clarification of the relations between physique and temperament will come about only by filling in the gap on the level between the anatomical and the psychological: that is, through the study of the physiological differences between people, a subject one might call *physiological anthropology*. The importance of such a study is really very obvious, yet curiously enough it has been much neglected. Partly the reason for this neglect has been, no doubt, the lack of a suitable classification of physique, in relation to which the physiological studies could be planned.

The first study of the physiological relations of the Sheldon components was reported in 1944 [9] when, in 50 healthy students, oral temperature and respiratory period at rest were found to correlate positively with ectomorphy and negatively with endomorphy. No correlation was apparent between the components and heart rate, cardiac output (ballistocardiograph method) and blood-pressure (except in so far as diastolic pressure was related to endomorphy because of the influence of arm width on both). It is of some interest that the two significant correlations of ectomorphy increased when the estimated leptosomic factor score was used instead of ectomorphy, and that this increase was somewhat more than that obtained by correcting the original correlations for broad categories. The leptosomic factor correlations were finally + 0·32 with respiratory rate and − 0·39 with oral temperature. A study of the partial correlations of oral temperature shows that when mesomorphy is held constant, the relation of leptosomic factor and temperature rises to − 0·52, and when the leptosomic factor is held constant, a relation of mesomorphy and temperature of + 0·43 appears. Both ectomorphy and mesomorphy independently make for a high oral temperature, the former more than the latter, at least in our sample. The mesomorphic ectomorphs have the highest temperatures, the ectomorphic mesomorphs the next highest. This is a rather crude observation but points the way, I think, to nicer studies of metabolic, endocrine and central nervous system differences. Older work has related various physiological variables to Kretschmer types or to indices such as the Pignet or simple Weight-divided-by-Height [10 to 16]. In the psycho-physiological field simple reaction time has been positively related to endomorphy and negatively to ectomorphy [17], and component dominance to certain ink-blot responses [41], and in the sphere of pathology some relations between disease and somatotypes [18], and neurosis and body build factors [19] have been reported. This study of physiological differences between adults is one uncharted approach to the subject.

A second approach seems equally promising; this is the study of human growth, or how the adult got to look that way. D'Arcy Thompson puts the relations of growth and physique most lucidly: "In short it is obvious that the *form* of an organism is determined by its rate of *growth* in various directions, hence rate of growth deserves to be studied as a necessary preliminary to the theoretical study of form, and organic form itself is found, mathematically speaking, to be a function of time" [20]. By reference to data already available on growth we can further clarify some of the relations of Sheldon's components and Burt's factors. The data we shall use are those of the Brush Foundation Study at Western Reserve [21] and of the Iowa Child Welfare Research Station [22].

The upper graph of fig. 3 shows growth in hip width of girls from birth to 17 years plotted simply as mean measurements of bitrochanteric diameter at each year of age. The lower graph shows exactly the same data as the upper, but plotted in a more informative manner. It is the *velocity* curve [23] of bitrochanteric diameter, showing how fast the tissues going to make hip width are growing. It is, in fact, the curve of the first derivative with regard to time of the upper curve. The points in the velocity curve are plotted as $\frac{\text{Bitroch.}t_2 - \text{Bitroch.}t_1}{t_2 - t_1}$. All the graphs to be presented are plotted in this form, $t_2 - t_1$ being one year. To bring the increments of different measurements to approximately the same scale, so as to be able to plot them on a single graph, every increment is divided by the adult mean value of the measurement in question. Thus the small increments of a small measurement are put on the same scale as the large increments of a larger measurement. The numerator is multiplied by 100 for convenience of scaling, making the final points to be given by $\frac{\text{Bitroch.}t_2 - \text{Bitroch.}t_1}{t_2 - t_1} \times \frac{100}{\text{Bitroch.}t_{17}}$, 17 years being taken as the adult value. The velocity of growth decreases from birth onwards, but at least two well-defined periods occur during which there is an upwards turn of the velocity curve, signifying an acceleration of growth. The larger of these two spurts is the better known, occurs in girls from about 9 years old to 13 and is called the *adolescent spurt*. The smaller of the two occurs from about 5½ to 7½ and may be called the *midgrowth spurt*.

I have taken the hip width as an example, because it takes part in *both* spurts, but the point is that by no means all measurements do so. Some diameters spurt at one time, some at another: the composition, we might say, of each spurt is different from that of the other. A person, then, who has a pronounced midgrowth spurt and a small adolescent spurt will end up different in form, supposing he started the same, from another individual who has a large adolescent but small midgrowth spurt. In precisely what ways he will be different we shall see presently: of course very great differences appear *before* the time of these spurts, which serve perhaps chiefly to put the finishing touches on to the physique. Fig. 4 shows the velocity curves of leg length and "trunk" length, or sitting height. From birth onwards the leg is growing in length faster than the trunk, until the time of the adolescent spurt. There is a marked difference between the two measurements at the adolescent spurt; leg length has a very small and minor spurt, while trunk length increases its velocity considerably. (The adolescent spurt in stature is, in fact, almost entirely due to growth of trunk; looked at from a biological point of view, stature is a queer compound measurement, of trunk and limb, and should be dropped.) Now it is here that we can, apparently, link up growth and Burt's body build factors. When the general factor of size, and the first bipolar, leptosomic, factor are accounted for, there remain at least four further well-defined group factors. One of these groups consists of the leg length measurements, as against a second which consists of trunk lengths. *It seems that these factors directly reflect relative growth rates as between leg and trunk occurring at the time of the adolescent spurt.*

This conclusion is supported, I think, by Mullen's most interesting study of the growth of factors from 7 to 17 [38]. Data for every other year of age were analysed separately by Holzinger's technique. Each age-group yields the same major factors; and there is also a further small group factor D_4 which represents trunk length. Now in the analysis of the 17-year-old girls D_4 is perfectly well marked, but as the ages get younger, so the identity of D_4 fades (that is its contribution to the total variance gets less and less), until at age 7 it is non-existent. It appears to emerge as separate from the limb and leptosome factors with the adolescent spurt, just when the growth curves diverge so radically.

We may become more ambitious, and look at the leptosomic factor itself. This is a very stable factor, in the sense that it has appeared in all Burt factor analyses in a very similar form [5, 6, 19, 24 and 28]. The chief negative saturations of this factor are with sitting height, leg length and arm length, and three of the chief positive saturations are with hip width, chest breadth and thigh circumference. We have growth data available for these six measurements, five of them being from the same subjects, with thigh girth from a different group. Fig. 5 shows the velocity curves; it is at once obvious that the lines in the upper half of the picture, which represent the length measurements, continue downwards from age 5½ to 7½, while the lines in the lower half, which represent breadths, turn upwards for a time. *That is, the length measurements do not take part in the midgrowth spurt, which is well marked for all the breadths.* We may surmise that the leptosomic factor refers at least in part to events of relative growth occurring at this time. These events, however, do not by any means account entirely for differences between individuals in ectomorphy or the leptosomic factor. Carter and Krause's analysis [37] of the Bakwin data [40] on new-born infants shows even at this age the presence of a well-marked bipolar leptosomic factor accounting for upwards of 10% of the variance, with similar saturations to those found in adults (with two interesting exceptions). Since growth is an exceedingly regular process [23], it seems reasonable to assume that those who are high in the leptosomic factor as infants are, by and large, high also as adults. Whatever the processes are, in fact, that control growth-to-the-ectomorphic-form, they are in operation already in fœtal life. There are times during post-natal growth when such processes are seen functioning most clearly—either because they exert larger effects at these times, or because they are less overlaid by other growth processes. Such a time in the genesis of ectomorphy seems to be the midgrowth period.

It does appear, then, that we can identify Burt's factors with events occurring *at certain times* during growth. The question raised earlier is answered—the factors *can* be reified, as physiological processes, and they should, accordingly, prove useful. The nature of the physiological processes the factors refer to is not yet clear. I am much more inclined to think factors reflect the *reactivity* of a set of tissues at a particular time—physiological fields, if you like—than the secretion of a particular hormone. The major control of these processes is, without any doubt, genetic; though how much environmental stresses at particular times can upset them is uncertain.

I have said nothing about the relations of Sheldon's components to growth, but what we have said of the leptosomic factor applies equally, of course, to ectomorphy. Endomorphy appears to be extremely similar to McCloy's factor I or fat factor [39], which has high saturations in subcutaneous tissue measurements, limb girths, and chest depth. (It looks as though the correspondence between McCloy's factor I and endomorphy is about the same as that of Burt's leptosomic factor and ectomorphy.) This factor is present in 9-day-old babies, and persists with varying importance throughout all the growth period. There is, particularly, one other of Sheldon's components whose relation to growth is, I feel, of great interest. This is the gynandromorphic component, or the component of femaleness of form in the male. Prior to the adolescent spurt, there is very little difference in growth pattern as between boys and girls. As is well known, the adolescent spurt of the girls occurs about two years before that of the boys, and is less pronounced in almost every measurement. The chief exception is pelvic width. Fig. 6 shows, above, the male and female spurts which characterize most measurements—here shoulder breadth is taken as a rather pronounced example—and, below, the exceptional hip width. The major relative growth velocity during the spurt is of the hips in girls, and of the shoulders in boys. What other sex differences of this sort occur during the spurt we do not know, but these relations of the shoulders and hips and the rest of the body, are the major attributes of Sheldon's feminine component. It seems sufficiently certain then that the gynandromorphic component arises at the adolescent spurt. An important piece of data from the Adolescent Growth Study of the University of California [29] carries us still further here. The time at which the adolescent spurt begins varies from person to person, and, as I have said already, girls spurt a couple of years earlier than boys. What Dr. Bayley found [29] was that the boys who had an early spurt had a spurt which resembled to some extent the spurt of girls. Conversely the late-spurting girls had spurts which resembled somewhat the usual spurt of boys. It seems—and there is other evidence in human growth to support the idea—that the way each tissue reacts to a hormonal stimulus common to all depends on its age. At any rate, what happens is that early-spurting boys come to have a higher degree of femininity than late-spurting ones. Now it seems probable that, given optimal environmental conditions, the time at which the spurt occurs is genetically determined; thus the phenomenon would be brought into relation with the familiar occurrence of intersexuality in lower animals. Further, if we assume that the relation Sheldon subjectively described between the feminine component of build and that of mind is correct, we can see the mechanism whereby some forms of homosexuality occur. That the relation postulated between femininity of physique and behaviour is indeed a close one has been shown by the work of the Grant Study of Harvard [30, 31, 32], and by the correlation found by Child and Sheldon between physique and Terman-Miles' masculinity-femininity score [33].

Thus a solution of some of the outstanding problems of physique and of personality does seem promised by the physiological approach. The difficulty lies entirely in obtaining access to normal people to study them. There is, as Sir Cyril Burt emphasized in a letter to *Nature* four years ago [34], the strongest need for the establishment in this country of a longitudinal, comprehensive and adequately-staffed study of the growth of healthy children.

REFERENCES

1 Sheldon, W. H. (1940) The Varieties of Human Physique. New York.

2 —— (1942) The Varieties of Temperament. New York.

3 Burt, C. (1940) The Factors of the Mind. London.

4 Mahalanobis, C. P. Paper read at Royal Anthropological Institute. December. 9, 1946. To be abstracted in *Man.*

5 Burt, C. (1944) The Factorial Study of Physical Types, *Man*, **72**, 82.

6 —— (1947) Paper read at Royal Anthropological Institute, October 15, 1946. To be published in *Ann. Eugen. Camb.*

7 Stevens, S. S. (1946) On the Theory of Scales of Measurement, *Science*, ***103***, *677.*

8 Thomson, G. H. (1946) The Factorial Analysis of Human Ability. London.

9 Tanner, J. M. (1944) Intercorrelations between Cardiovascular Variables in Healthy Men and the Relation of Physique to these and other Variables. *Proc. Physiol. Soc. Philad., Amer. J. med. Sci.*, **207**, *684.*

10 Miassnikov, A. L. (1927) Beiträge zur Konstitutionsforschung, II Blutcholesterol und Konstitution, *Z. klin. Med.*, **105**, 228.

11 Tschernorutzky, M. W. (1929-31) Wechselsbeziehung zwischen Funktionseigenschaften und Konstitutionstypus. *Z. KonstLehre*, **15**, 134.

12 Peterson, W. F., and Levinson, S. A. (1930) The Skin Reactions, Blood Chemistry and Physical Status of "Normal" Men, and of Clinical Patients, *Arch. Path.*, **9**, 157.

13 Gildea, E. F., Kahn, E., and Man, E. B. (1936) The Relationship between Body Build and Serum Lipids and a Discussion of These Qualities as Pyknophilic and Leptophilic Factors in the Structure of the Personality, *Amer. J. Psychiat.*, **92**, 1247.

14 Seltzer, C. C. (1940) Body Build and Oxygen Metabolism at Rest and During Exercise, *Amer. J. Physiol.*, **129**, 1.

15 Wenger, M. A. (1943) An Attempt to Appraise Individual Differences in Level of Muscular Tension, *J. exp. Psychol.*, **32**, 213.

16 Jokl, E. (1946) Height, Weight and Body Index of School Children. A Correlation Study, *Growth*, **10**, 1.

17 Smith, H. C. and Boyarsky, S. (1943) Relationship Between Physique and Simple Reaction Time. *Character and Personality*, **12**, 46.

18 Draper, G., Dupertuis, C. W., and Caughey, J. L. (1944) Human Constitution in Clinical Medicine. New York.

19 Rees, W. L., and Eysenck, H. J. (1945) A Factorial Study of Some Morphological and Psychological Aspects of Human Constitution, *J. ment. Sci.*, **91**, 8.

20 Thompson, D'A. W. (1942) On Growth and Form. London.

21 Simmons, K. (1944) The Brush Foundation Study of Child Growth and Development, II Physical Growth and Development, *Monographs for Soc. Research in Child Development*, **9**, 1.

22 Boynton, B. (1936) The Physical Growth of Girls. A Study of the Rhythm of Physical Growth from Anthropometric Measurements on Girls between Birth and Eighteen Years, *Univ. of Iowa Studies in Child Welfare*, **12**, No. 4.

23 Count, E. W. (1943) Growth Patterns of the Human Physique: An Approach to Kinetic Anthropometry, *Human Biol.*, **15**, 1.

24 Cohen, J. I. (1938) Determinants of Physique, *J. ment. Sci.*, **84**, 495.

25 —— (1940) Physical Types and Their Relation to Psychotic Types, *J. ment. Sci.*, **86**, 602.

26 —— (1941) Physique, Size and Proportions, *Brit. J. med. Psychol.*, **18**, 323.

27 Holzinger, K. J., and Harman, H. H. (1941) Factor Analysis. Chicago.

28 Hammond, W. H. (1942) An Application of Burt's Multiple General Factor Analysis to the Delineation of Physical Types, *Man*, **42**, 4.

29 Bayley, N. (1943) Size and Body Build of Adolescents in Relation to Rate of Skeletal Maturing, *Child Develpm.*, **14**, 47.

30 Seltzer, C. C., and Brouha, L. (1943) The "Masculine" Component and Physical Fitness. *Amer. J. phys. Anthrop.*, N.S. **1**, 95.

31 —— (1945) The Relationship Between the Masculine Component and Personality, *Amer. J. phys. Anthrop.*, N.S. **3**, 33.

32 Woods, W. L., Brouha, L., and Seltzer, C. C. (1943) The Selection of Officer Candidates. Harvard Univ. Press.

33 Child, I. L., and Sheldon, W. H. (1941) The Correlation Between Components of Physique and Scores on Certain Psychological Tests, *Character and Personality*, **10**, 23.

34 Burt, C. (1943) Factorial Analysis of Physical Growth, *Nature*, **152**, 75.

35 —— (1938) The Analysis of Temperament, *Brit. J. med. Psychol.*, **17**, 518.

36 Marshall, E. L. (1936) A Multiple Factor Study of 18 Anthropometric Measurements of Iowa City Boys, *J. exp. Educ.*, **5**, 212.

37 Carter, H. D., and Krause, R. H. (1936) Physical Proportions of the Human Infant, *Child Develpm.*, **7**, 60.

38 Mullen, F. A. (1940) Factors in the Growth of Girls, *Child Develpm.*, **11**, 27.

39 McCloy, C. H. (1940) An Analysis for Multiple Factors of Physical Growth at Different Age Levels, *Child Develpm.*, **11**, 249.

40 Bakwin, H. and Bakwin, R. M. (1943) Body Build in Infants, V Anthropometry of Newborn, *Hum. Biol.*, 6, 612.

41 Fiske, D. W. (1944) A Study of Relationship to Somatotype, *J. applied Psychol.*, **28**, 504.

Sir Cyril Burt: Dr. Tanner has rightly drawn attention to the valuable assistance that may be gained, not only by medicine generally, but by psychiatry in particular, from the application of factor-analysis to the study of its problems. It is commonly supposed that psychologists introduced factorial methods solely to study mental abilities; but in this country such methods were applied almost from the outset to the investigation of physical and temperamental data. It is a method that is always appropriate wherever the phenomena to be investigated depend on a large number of inter-related variables which cannot as yet be disentangled by observational or experimental devices. It thus seems peculiarly suited to the study of neurotic and psychotic disorders.

I should, however, like to emphasize its limitations. It is of value chiefly in preliminary inquiries for confirming or modifying hypotheses relating to classification; it cannot claim to be a substitute for experimental research or clinical observation.

I think, too, that Dr. Tanner has rightly indicated that the best starting-point is to be found in the examination of physical characteristics. He has, I imagine, chosen the topic of body-types because they are supposed to be associated with certain temperamental and psychopathological tendencies. In this field, the best-known work, but by no means the most scientific, is that of Kretschmer. The doctrine is as old as Hippocrates: but scientific interest in the subject began with British physicians about a century ago—Addison, Laycock, Hutchinson and others, who were all largely influenced by the early work of Hunter. Their writings prompted the investigations of the French school; and it was from these in turn that Kretschmer derived his views. But, as Professor Major Greenwood pointed out, the most careful Continental work has been that of the school of clinical anthropology established at Padua by Di Giovanni.

In this country the attempt to investigate the problem by factorial methods began with studies of physical and temperamental measurements among school children. But the most extensive data have been provided by material collected during the recent war. In the R.A.F., over 30,000 men have been measured; and, at almost every age and nationality, the same two prominent factors appear—first the general factor of size, and secondly the bipolar factor contrasting growth in the long bones with transverse or circumferential growth.

The first or general factor has been studied particularly in connexion with attempts to assess nutrition; but it is the second or bipolar factor that is of interest to the psychiatrist. This appears definitely to confirm the old notion of the *habitus phthisicus* as contrasted with the *habitus apoplecticus*; and it is of interest to note that the former has proved to be significantly correlated, not only with tendencies to tubercular disease, but also with gastric and duodenal ulcer; while the latter is significantly correlated, not only with arteriosclerosis, coronary occlusion and allied vascular disorders, but also with diseases of the gall-bladder. The association with contrasted temperamental tendencies has turned out to be less marked than earlier writers supposed: it is both positive and significant, but, so far as evidence goes at present, far too small to be of practical use for diagnostic purposes.

It is extremely valuable to have heard a discussion of Sheldon's methods from one who has had the advantage of studying those methods at first hand. The methods themselves seem to me to be excellent. But I feel very dubious about the hypothesis on which Sheldon's nomenclature is based—the embryological hypothesis embodied in the terms ectomorphic, mesomorphic, and endomorphic.

To discover what are the real causal factors at work, a mere statistical analysis alone cannot suffice. Factor-analysis has been applied to growth-rates among school children; and has fully confirmed the distinction between what Julian Huxley and his co-workers have called isometric and allometric growth. The fluctuations of physical growth can be admirably exhibited by fitting the measurements obtained from children at successive ages by means of a generalized logistic curve: the results strongly suggest that the body-types observable among adults are produced by characteristic differences in the growth-rates for different parts of the body.

There is, however, an urgent need to supplement the results of these preliminary statistical inquiries by investigations along other lines in order to determine what part is played by genetic, biochemical, endocrinological factors and the like, in determining both body-type and the temperamental and psychopathic tendencies that appear to be indirectly correlated with it. Meanwhile, the data which Dr. Tanner has described and analysed form a most valuable contribution to our knowledge.

Section of Odontology

President—Professor H. STOBIE, F.R.C.S., L.D.S.E.

[*November* 25, 1946]

Severe Infections of the Mandible

By D. GREER WALKER, M.B., M.Dent.Sc.

I SHALL confine my paper to the treatment of severe mandibular infections. In this review of over 150 cases I propose to discuss the relative merits of surgery and penicillin.

Vaughan Hudson (1946) stated: "Our method of treatment, however, in all cases of acute osteomyelitis was to institute penicillin and wait and observe the progress of the case. It soon became apparent that penicillin swept the organism from the blood-stream and reduced the acute lesion to a chronic lesion. The subsequent fate of the patient depended upon the management of this now chronic osteomyelitis." He makes a further interesting statement on local penicillin: "Local penicillin as an adjunct to systemic penicillin made no difference to the results. In fact the recurrence rate when penicillin was used in addition to systemic penicillin was statistically higher than in those who had systemic penicillin only." Butler (1946) made the following observation: "We no longer consider it necessary to interfere with the primary focus of infection unless there is a local collection of pus."

What is the role that penicillin is to play in severe mandibular infections? Are we to use it alone or in conjunction with surgery as described by Mowlem (1944). Speaking about radical surgery recently Henry (1946) has stated: "The advent of first the sulphonamides and then penicillin has changed our conception of the disease and given radical surgery a degree of safety that was not formerly contemplated." This is true and there is no doubt that surgery is essential in the treatment of chronic osteomyelitis, but I agree with Vaughan Hudson that the best method of treating acute cases is to institute systemic penicillin and wait and observe the progress. To discuss the treatment of these severe infections a clear idea of the various types is essential and I have adopted the following classification:

(1) *Acute infections.*—(*a*) Involving chiefly the soft tissues, e.g. submandibular abscess; (*b*) involving chiefly the bone, i.e. osteomyelitis; (*c*) occurring in children.

(2) *Chronic infections of the mandible.*—(*a*) Involving a local area, e.g. local necrosis; (*b*) involving a diffuse area, e.g. chronic osteomyelitis; (c) involving the condyloid and coronoid processes, and the temporomandibular joint.

(3) *Infections of cystic origin, e.g. solitary cyst of the ramus.*

(4) *Infections occurring in bone that is already affected by some pathological disease.*—(*a*) Where the pathological condition is limited to the mandible, e.g. sclerosed mandible; (*b*) where the pathological condition involves the other facial bones or the entire skeleton, e.g. Albers-Schönberg disease.

(5) *Specific infections, e.g. actinomycosis.*

(6) *Malignant disease, e.g. post-radium necrosis.*

(1*a*) *Acute infections of the soft tissues, e.g. submandibular abscess.*—The very rapidly spreading cellulitis of the neck scarcely comes within the framework of this paper. Fortunately much more common are the localized infections arising from some dental cause, or, perhaps less often, of traumatic origin following infection of a fracture. The removal of mandibular teeth will not drain or stem the advance of an acute infection which has passed from the immediate vicinity of the roots of the teeth. Frequently patients appear at hospital with the familiar dental abscess and offer the history that a tooth has been removed, teeth fractured in attempted removal, &c., and in spite of this treatment the abscess has continued to increase in size. The correct treatment of all these abscesses in the early stages has been the application of heat externally and intra-orally. When the presence of pus was established a submandibular incision was made with good dependent drainage. This treatment in the past has produced excellent results. Nowadays the use of penicillin instituted early in the treatment of these acute infections prevents many an acute abscess, or a severe bone infection. So often the infection has progressed for some days and is beyond hope of complete resolution. In such cases where penicillin is given the abscess may be incised and drained, or the pus evacuated and some penicillin placed in the abscess cavity without dependent drainage. At present I prefer to employ dependent drainage for a short time rather than a primary suture; the degree of recovery has been more rapid when penicillin has been given and the old principles of surgery employed. Following the control of the acute infection the cause must be removed. I, like many others, advocate this after the acute infection has subsided. Before passing to the bony infections we ought to consider the dental abscess in which the cause is not always apparent at the time. I have seen on occasions what appears to be a subperiosteal abscess and on careful examination no cause can be found. Whatever the ætiology the abscess must be treated as already outlined and if no cause is found on further thorough examination the case should be observed at periodic intervals. Sooner or later the cause will come to light and can be removed.

(1*b*) *Acute infections of bone, acute osteomyelitis.*—It is rather surprising that infection giving rise to alveolar abscesses does not more often invade the bone to a greater degree. The infection seems to pass rapidly out of the bone into the soft tissues. This is very fortunate as the more widespread infection of bone causes greater difficulties in treatment. Acute infection of the bone has been labelled for many years "acute osteomyelitis"; let us not linger to discuss terminology but rather the treatment at present employed. The first method, introduced by *Mowlem* [3], a radical removal of bone coupled with the administration of penicillin, has proved effective. The second, the use of penicillin systemically without surgical interference will be the method of choice in the future. If the organisms are sensitive to penicillin I fail to see the need of surgery apart from the possible treatment of a residual infection. The first case that I treated without surgery was in 1944 when a patient was admitted to Stoke Mandeville Hospital with an acute infection of the mandible extending from one molar region to the other on the opposite side. This had resulted from the extraction of a premolar tooth. All the clinical signs of an acute osteomyelitis were present and radiological signs were just becoming evident. I discussed the case with Professor McIntosh and we decided to try the effect of sulphathiazole immediately. The following course was given:

(i) 2 grammes stat followed by 1·5 grammes four-hourly for three days; (ii) 1 gramme four-hourly for two days; (iii) 1 gramme six-hourly for two days. The total dose of sulphathiazole was 46·5 grammes over a period of seven days. All pain ceased after two days and all signs of clinical infection vanished within the week. The only signs of infection lay in the subsequent radiographs which showed the typical decalcification (fig. 1). The complete recovery of this case without surgery led us to adopt the same lines of treatment with the introduction of penicillin. The same result is true of cases treated by penicillin. The time factor is most important if complete resolution is to be obtained without recourse to surgery. Cases not seen early will undoubtedly need treatment for some residual infection. Penicillin used in these cases will, however, limit considerably the extent of the infection. I find it rather early to be dogmatic but the results so far more than justify the omission of surgery in the early stages of acute mandibular infections.

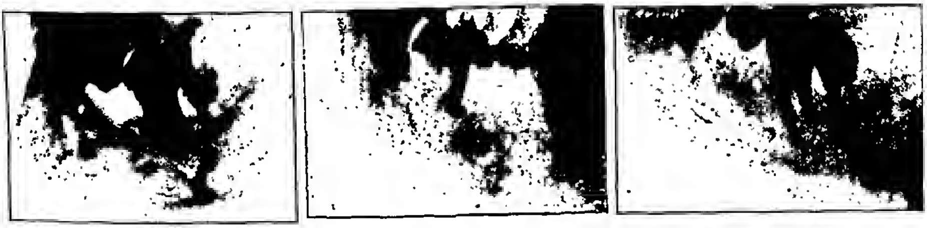
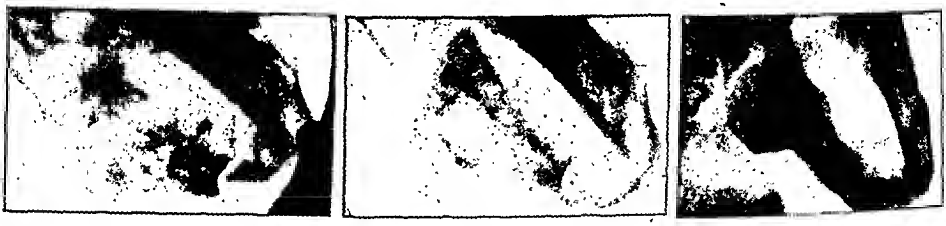

16.7.44. 16.8 44. 1.11.44.

FIG. 1.—*Acute osteomyelitis of the mandible.*—16.7.44: V. E., aged 31. Admitted to hospital. Early bone changes are just discernible on the radiographs. 18.7.44: Sulphathiazole course commenced. 24.7.44: Course completed; total dose 46·5 grammes. 16.8.44: Decalcification well marked on the radiographs. No clinical signs of infection remain. Discharged from hospital. 1.11.44: Out-patient radiographs show some decalcification still present along the lower border of the mandible. 23.11.46: No clinical or radiological signs of any residual infection.

(1*c*) *Acute infections occurring in children.*—The treatment of acute abscesses and acute bone infections occurring in children is similar to that already described for adults but there are two points that I should like to mention. The first concerns acute abscesses: There should be no hesitation in establishing early dependent drainage. If the infection is not controlled and is allowed to continue the inevitable result is a maldevelopment of the affected portion of the jaw. It is a pathetic deformity in an otherwise normal child. The second point relates to acute bone infections: The response of the young bone to infection is usually very good and the same holds true for the reaction of the teeth to such an infection. More than ever I feel that penicillin is indicated in these cases and surgery reserved for any residual infection. When it is necessary to perform a sequestrectomy great care should be taken so that the new bone is not removed nor the vital teeth disturbed or extracted. Failure to bear these points in mind will lead to gross deformities.

(2*a*) *Chronic infection of the mandible involving a local area.*—The commonest causes of local infection are a dead tooth or a retained root. This residual infection causes more frequently an intra-oral and less often an extra-oral sinus. There are other causes for which the teeth have been extracted and the socket has undergone varying degrees of necrosis. This may vary from the typical shedding of alveolar sequestra to the more extensive necrosis that may result in a pathological fracture (fig. 2). The removal of teeth has not prevented the infection from becoming chronic.



21.11.44. 5.12.44. 11.4.45.

FIG. 2.—*Pathological fracture of the mandible.*—21.11.44: M. E., aged 44. Admitted to hospital with multiple discharging sinuses in the lower right molar region and one external sinus below the lower border of the mandible. Radiographs showed a pathological fracture and multiple sequestra present. 28.11.44: Sequestrectomy performed intra-orally. 20,000 units of penicillin were given twenty-four hours prior to the operation and continued four-hourly. Local penicillin was applied on the intra-oral packing. 30.11.44: Packing changed and more local penicillin applied. Wound clean. 1.12.44: Systemic penicillin stopped. Local penicillin continued on daily changes of the packing. 15.12.44: Packing stopped, wound now well healed. 18.12.44: Discharged from hospital. 11.4.45: Seen as an out-patient; no signs of clinical infection present and radiological examination reveals good recalcification.

In treating these chronic infections the remaining portions of teeth and dead bone must be removed. There is little need to lay down hard and fast rules as to whether sequestrectomies should be performed intra-orally or extra-orally. It is obvious that it is preferable that the operation should be intra-oral but there are occasions when the method of choice must be external. Previous to the introduction of penicillin one saucerized the cavities in the bone following the removal of the dead bone. The cavities were packed for a short period. I think the same holds good to-day for operations inside the mouth when we use systemic penicillin. I have not observed any additional improvement in the cases where local penicillin has also been used. For external operations there is little need to pack the cavity when penicillin is given systemically. Where a good débridement has been performed suture of the wound is preferable to leaving it open.

(2*b*) *Chronic infections of the mandible involving a diffuse area.*—It is to be hoped that we shall no longer see the end-results of acute osteomyelitis with the multiple sequestra and areas of sclerosed bone. The following illustrates well a long-established infection of the mandible of some eighteen months' duration: Multiple sequestra were present causing several discharging external sinuses. Sequestra and teeth had been removed on a number of occasions with no improvement. The case was then diagnosed as actinomycosis following a positive report from the laboratory. When admitted to Stoke Mandeville Hospital we were unable to confirm the previous laboratory findings and it was felt that, apart from the multiple sinuses, the clinical picture did not resemble actinomycosis. In such cases extensive submandibular incisions are essential to open all areas of infection. In these cases I have given systemic penicillin, but it is doubtful of how much value this may be when the mandible is sclerosed. On account of this I have been rather reluctant to stitch the submandibular incisions immediately. I have felt the wiser course with our present knowledge is packing of the external wounds and by this method local penicillin can be applied. I am rather doubtful of the value of local penicillin in these cases. With less extensive infections and of a shorter duration it is preferable to close the external wounds on completing the operation.

The above case demonstrates very well the response on the part of the tissues to the invading infection. On rare occasions this reaction to infection seems to be completely absent. Fig. 3 is an example of the loss of almost the entire mandible. The radiograph shows the destruction of the bone. There seems to be no response on the part of the bone to deal with the infection. The history was most obscure but one could safely say that such a necrosis might well have been the result of phosphorus. With our present knowledge there is little that we can do when there is no response on the part of the bone. .

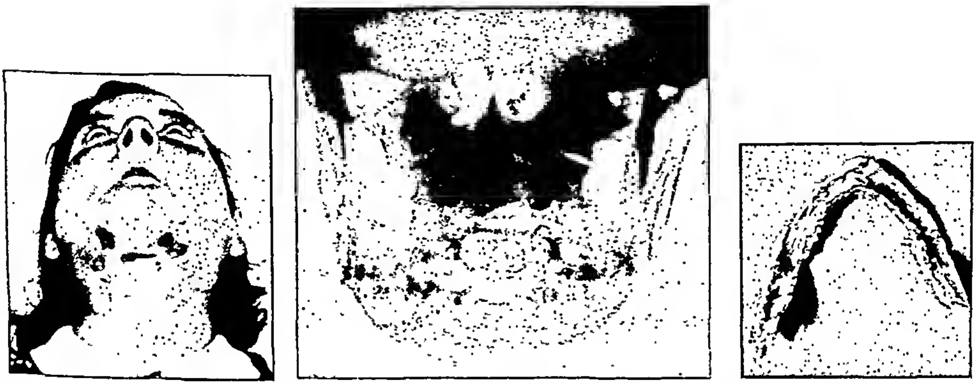
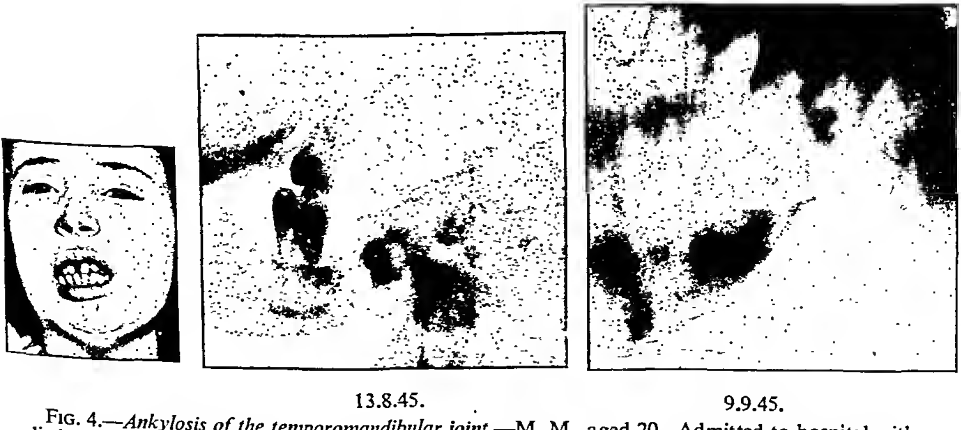


FIG. 3.—*Loss of almost the entire mandible.*—G. A., aged 41. Admitted to hospital with multiple submandibular and intra-oral sinuses. The radiograph shows the extensive involvement of bone. Shortly after admission practically the entire mandible was removed in one piece. It began to present through the alveolar mucosa as a sequestrum and was removed via the mouth.

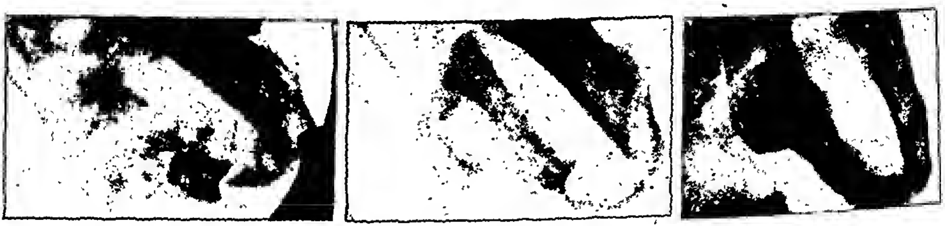
(2*c*) *Chronic infections involving the condyloid and coronoid processes and the temporomandibular joint.*—There seem to be two types of cases both of which eventually produce an ankylosis of the temporomandibular joint. The one is an ascending infection which starts in the region of the third molar and for some reason or other extends upwards to invade the joint. The other appears to originate from middle-ear infection and to spread towards the joint, condyle and coronoid process. Fig. 4



13.8.45. 9.9.45.

FIG. 4.—*Ankylosis of the temporomandibular joint.*—M. M., aged 20. Admitted to hospital with a discharging external sinus of some fifteen years' duration. The photograph shows the limitation of the temporomandibular joint, the first radiograph the infection around the molar teeth. Both teeth were removed via the mouth and in so doing the mandible was fractured. The tomograph shows the position of the fragments and a considerable loss of bone. This undoubtedly freed the mandible but the much sounder treatment would be the removal of bone higher in the ramus as was originally planned for the treatment of this case.

varying degrees of necrosis. This may vary from the typical shedding of alveolar sequestra to the more extensive necrosis that may result in a pathological fracture (fig. 2). The removal of teeth has not prevented the infection from becoming chronic.



21.11.44. 5.12.44. 11.4.45.

FIG. 2.—*Pathological fracture of the mandible.*—21.11.44: M. E., aged 44. Admitted to hospital with multiple discharging sinuses in the lower right molar region and one external sinus below the lower border of the mandible. Radiographs showed a pathological fracture and multiple sequestra present. 28.11.44: Sequestrectomy performed intra-orally. 20,000 units of penicillin were given twenty-four hours prior to the operation and continued four-hourly. Local penicillin was applied on the intra-oral packing. 30.11.44: Packing changed and more local penicillin applied. Wound clean. 1.12.44: Systemic penicillin stopped. Local penicillin continued on daily changes of the packing. 15.12.44: Packing stopped, wound now well healed. 18.12.44: Discharged from hospital. 11.4.45: Seen as an out-patient; no signs of clinical infection present and radiological examination reveals good recalcification.

In treating these chronic infections the remaining portions of teeth and dead bone must be removed. There is little need to lay down hard and fast rules as to whether sequestrectomies should be performed intra-orally or extra-orally. It is obvious that it is preferable that the operation should be intra-oral but there are occasions when the method of choice must be external. Previous to the introduction of penicillin one saucerized the cavities in the bone following the removal of the dead bone. The cavities were packed for a short period. I think the same holds good to-day for operations inside the mouth when we use systemic penicillin. I have not observed any additional improvement in the cases where local penicillin has also been used. For external operations there is little need to pack the cavity when penicillin is given systemically. Where a good débridement has been performed suture of the wound is preferable to leaving it open.

(2*b*) *Chronic infections of the mandible involving a diffuse area.*—It is to be hoped that we shall no longer see the end-results of acute osteomyelitis with the multiple sequestra and areas of sclerosed bone. The following illustrates well a long-established infection of the mandible of some eighteen months' duration: Multiple sequestra were present causing several discharging external sinuses. Sequestra and teeth had been removed on a number of occasions with no improvement. The case was then diagnosed as actinomycosis following a positive report from the laboratory. When admitted to Stoke Mandeville Hospital we were unable to confirm the previous laboratory findings and it was felt that, apart from the multiple sinuses, the clinical picture did not resemble actinomycosis. In such cases extensive submandibular incisions are essential to open all areas of infection. In these cases I have given systemic penicillin, but it is doubtful of how much value this may be when the mandible is sclerosed. On account of this I have been rather reluctant to stitch the submandibular incisions immediately. I have felt the wiser course with our present knowledge is packing of the external wounds and by this method local penicillin can be applied. I am rather doubtful of the value of local penicillin in these cases. With less extensive infections and of a shorter duration it is preferable to close the external wounds on completing the operation.

The above case demonstrates very well the response on the part of the tissues to the invading infection. On rare occasions this reaction to infection seems to be in such conditions a sequestration can be a very lengthy process. The radiographs show the progress of the infection and the remarkable growth of new bone. An interesting observation in this case was the remarkable effect of penicillin on the soft-tissue infections as opposed to intra-osseous infection. In the early stages of the acute bone infection penicillin had no effect, but later in the treatment the patient developed a severe submandibular infection which was rapidly controlled by penicillin. I think there is some justification in these cases for not performing any major surgical operations.

(5) *Specific infections, e.g. actinomycosis.*—Up to now I have considered what might be described as pyogenic infections in and around the mandible. Specific infections involving the mandible are rare; the commonest of this group is actinomycosis. MacGregor [6] has pointed out the advantages of penicillin in treating this infection and I feel that I can add little to what has already been said. The place of surgery in the treatment of these conditions is confined to incising abscesses or less often to a débridement when the mandible is actually involved. Fig. 6 demonstrates such a case treated by penicillin and surgery. There has been no recurrence of the infection.

The treatment of these cases cannot be dismissed without laying stress on the excellent results of X-ray therapy. Fig. 7 shows a case treated entirely by radiotherapy. It would appear that the method of choice at present is a combination of X-ray therapy and penicillin.

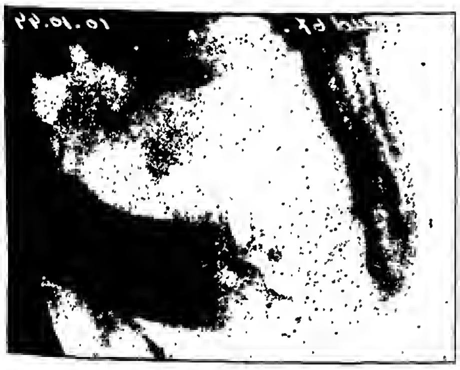
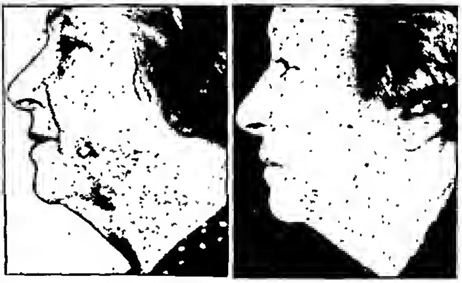


FIG. 6. A. L. Male



7.9.44. 30.10.46.

FIG. 7.

FIG. 6.—*Actinomycosis involving the mandible.*—There was a history that some lower incisors had been extracted and the abscess which had been present continued to increase in size. When admitted to hospital there were discharging submental sinuses and the clinical picture was very unlike a dental abscess. The radiographs showed considerable infection in the incisor region. 20,000 units of penicillin were given four-hourly and a débridement performed. Dr. J. Murray confirmed the diagnosis from tissue removed at this operation. The penicillin was continued for six days. In spite of the good result obtained we should now increase the dose of penicillin, give it three-hourly, and over a longer period.

FIG. 7.—*Actinomycosis involving the soft tissues.*—B. D., aged 59. Admitted to hospital with what appeared to be a dental abscess. The only history obtained was the loss of a crown from ⌈5 and soon after this the abscess appeared. The diagnosis of actinomycosis was confirmed by Dr. R. Robinson and the case transferred for X-ray therapy (Middlesex Hospital). The following course was given:—

Course completed over two areas in 16 treatments spread over eighteen days. Size of field 6×8 cm.; dist: 40 cm.; kV. 220; Ma. 10; ½ value layer 2·1 mm. of Cu. Filter, Thoræus. Dosage rate 45 r/minute.

(1) Lesion direct, 3,000 r.
(2) Lesion from above 200 r.
Total time 67′ 45″.

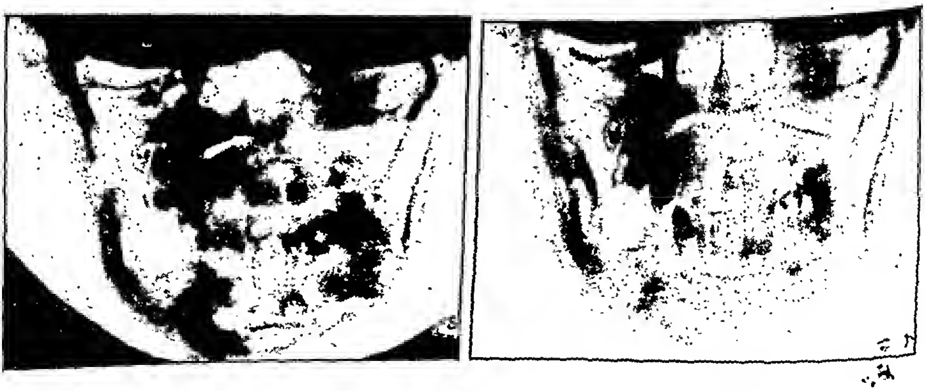
The second photograph shows the result two years later. No penicillin was given.

demonstrates the end-result of an acute abscess fifteen years ago. There is complete ankylosis of the temporomandibular joint. The external sinus is still discharging and no doubt caused by the infection around the molar teeth. The treatment in these cases is twofold. In the first instance any source of infection must be removed and when this has been dealt with, the ankylosis treated by extensive removal of the upper portion of the ramus together with its two processes.

(3) *Infections of cystic origin, e.g. solitary cyst of the ramus.*—The majority of cysts when they become infected cause little difficulty from the treatment point of view, but the solitary cyst involving the ramus, when infected, can be very troublesome. A marked degree of trismus in the acute stage of the infection prevents early operation and in such cases penicillin is more than helpful. The operation for these cysts lying high in the ramus is by no means a simple problem as I have stated in a previous paper [5]. There is a tendency for recurrence, particularly of the infection, if the orifice of the cyst is not kept patent with a skin graft.

(4*a*) *Infections occurring in bone that is already affected by some pathological disease—limited to the mandible.*—The type of case that I wish to describe here is by no means common. The mandible is for some reason of a sclerotic nature, a patient has a tooth removed and some infection follows. After the acute stage a very long process begins in which there seems to be a very low-grade infection present. The patient does not complain of any severe symptoms nor are they completely absent. The problem is whether to leave well alone or to interfere. What can penicillin do in these cases? It is doubtful if it is of much value. Is surgery worth while? The problem confronting us is the exact extent of the sclerosed bone and upon how much there is superimposed the new infection. As the boundaries are so ill-defined one hesitates to tackle the problem surgically. As these conditions occur in older patients the natural trend is to avoid surgery if possible.

(4*b*) *Infection occurring in bone that is already affected by some pathological disease—not limited to the mandible.*—These types of cases might be said to be even more rare than what we have just considered. To illustrate this group of cases I shall confine myself to one example, Albers-Schönberg disease, in which the problem of infection can be indeed very great. Fig. 5 demonstrates very well how



30.11.45. 11.9.46.

FIG. 5.—*Infection of the right mandible occurring in a case of "marble bones".*—Admitted to hospital with pain in the $\overline{8765}|$ region. The molars and premolar were extremely *tender and loose*, and had to be extracted. A lengthy process of infection then set in and the first radiograph shows the laying down of new bone, and the second—almost one year later—practically *complete separation* of the dead bone (*see Proc. R. Soc. Med.* (1938) 32, 282).

in such conditions a sequestration can be a very lengthy process. The radiographs show the progress of the infection and the remarkable growth of new bone. An interesting observation in this case was the remarkable effect of penicillin on the soft-tissue infections as opposed to intra-osseous infection. In the early stages of the acute bone infection penicillin had no effect, but later in the treatment the patient developed a severe submandibular infection which was rapidly controlled by penicillin. I think there is some justification in these cases for not performing any major surgical operations.

(5) *Specific infections, e.g. actinomycosis.*—Up to now I have considered what might be described as pyogenic infections in and around the mandible. Specific infections involving the mandible are rare; the commonest of this group is actinomycosis. MacGregor [6] has pointed out the advantages of penicillin in treating this infection and I feel that I can add little to what has already been said. The place of surgery in the treatment of these conditions is confined to incising abscesses or less often to a débridement when the mandible is actually involved. Fig. 6 demonstrates such a case treated by penicillin and surgery. There has been no recurrence of the infection.

The treatment of these cases cannot be dismissed without laying stress on the excellent results of X-ray therapy. Fig. 7 shows a case treated entirely by radiotherapy. It would appear that the method of choice at present is a combination of X-ray therapy and penicillin.

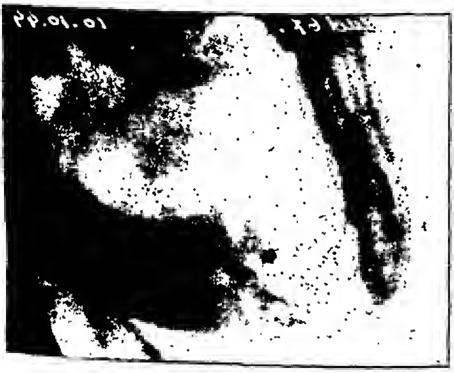
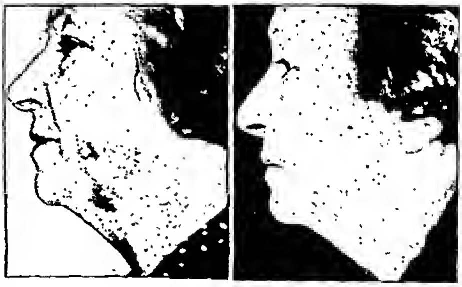


FIG. 6. A. L. Male



7.9.44. 30.10.46.

FIG. 7.

FIG. 6.—*Actinomycosis involving the mandible.*—There was a history that some lower incisors had been extracted and the abscess which had been present continued to increase in size. When admitted to hospital there were discharging submental sinuses and the clinical picture was very unlike a dental abscess. The radiographs showed considerable infection in the incisor region. 20,000 units of penicillin were given four-hourly and a débridement performed. Dr. J. Murray confirmed the diagnosis from tissue removed at this operation. The penicillin was continued for six days. In spite of the good result obtained we should now increase the dose of penicillin, give it three-hourly, and over a longer period.

FIG. 7.—*Actinomycosis involving the soft tissues.*—B. D., aged 59. Admitted to hospital with what appeared to be a dental abscess. The only history obtained was the loss of a crown from ⌈5 and soon after this the abscess appeared. The diagnosis of actinomycosis was confirmed by Dr. R. Robinson and the case transferred for X-ray therapy (Middlesex Hospital). The following course was given:—

Course completed over two areas in 16 treatments spread over eighteen days. Size of field 6×8 cm.; dist: 40 cm.; kV. 220; Ma. 10; ½ value layer 2·1 mm. of Cu. Filter, Thoræus. Dosage rate 45 r/minute.

(1) Lesion direct, 3,000 r.
(2) Lesion from above 200 r.
Total time 67′ 45″.

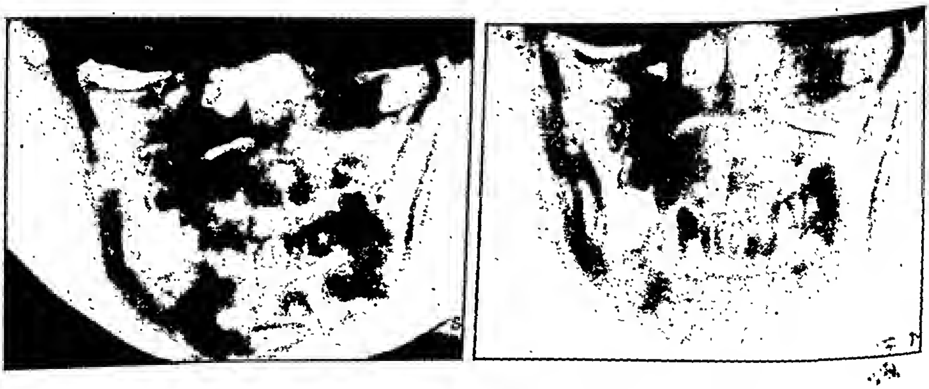
The second photograph shows the result two years later. No penicillin was given.

demonstrates the end-result of an acute abscess fifteen years ago. There is complete ankylosis of the temporomandibular joint. The external sinus is still discharging and no doubt caused by the infection around the molar teeth. The treatment in these cases is twofold. In the first instance any source of infection must be removed and when this has been dealt with, the ankylosis treated by extensive removal of the upper portion of the ramus together with its two processes.

(3) *Infections of cystic origin, e.g. solitary cyst of the ramus.*—The majority of cysts when they become infected cause little difficulty from the treatment point of view, but the solitary cyst involving the ramus, when infected, can be very troublesome. A marked degree of trismus in the acute stage of the infection prevents early operation and in such cases penicillin is more than helpful. The operation for these cysts lying high in the ramus is by no means a simple problem as I have stated in a previous paper [5]. There is a tendency for recurrence, particularly of the infection, if the orifice of the cyst is not kept patent with a skin graft.

(4*a*) *Infections occurring in bone that is already affected by some pathological disease—limited to the mandible.*—The type of case that I wish to describe here is by no means common. The mandible is for some reason of a sclerotic nature, a patient has a tooth removed and some infection follows. After the acute stage a very long process begins in which there seems to be a very low-grade infection present. The patient does not complain of any severe symptoms nor are they completely absent. The problem is whether to leave well alone or to interfere. What can penicillin do in these cases? It is doubtful if it is of much value. Is surgery worth while? The problem confronting us is the exact extent of the sclerosed bone and upon how much there is superimposed the new infection. As the boundaries are so ill-defined one hesitates to tackle the problem surgically. As these conditions occur in older patients the natural trend is to avoid surgery if possible.

(4*b*) *Infection occurring in bone that is already affected by some pathological disease—not limited to the mandible.*—These types of cases might be said to be even more rare than what we have just considered. To illustrate this group of cases I shall confine myself to one example, Albers-Schönberg disease, in which the problem of infection can be indeed very great. Fig. 5 demonstrates very well how



30.11.45. 11.9.46.

FIG. 5.—*Infection of the right mandible occurring in a case of "marble bones".*—Admitted to hospital with pain in the $\overline{8765|}$ region. The molars and premolar were extremely tender and loose, and had to be extracted. A lengthy process of infection then set in and the first radiograph shows the laying down of new bone, and the second—almost one year later—practically complete separation of the dead bone (*see Proc. R. Soc. Med.* (1938) 32, 282).

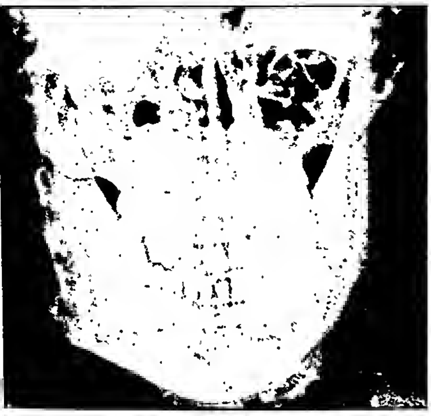


FIG. 1.

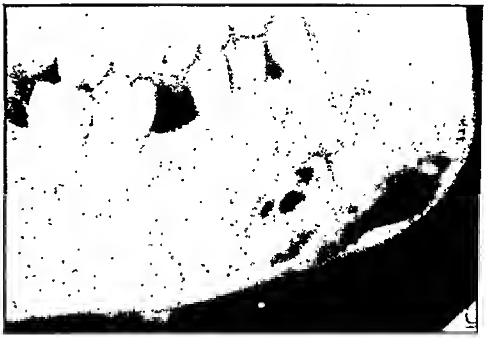
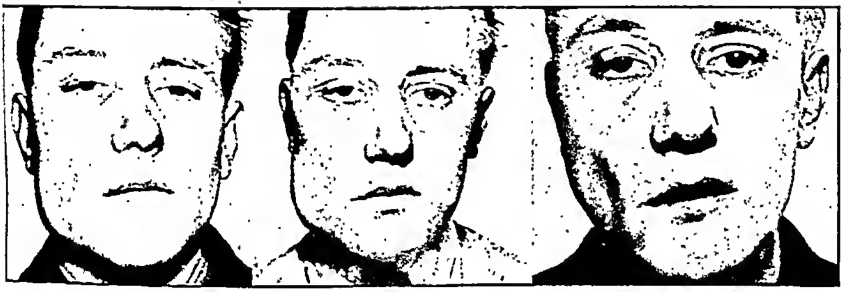


FIG. 2.



(a) (b) Two years later. (c) After operation.

FIG. 3.

CASE I. [Figs. 1, 2, 3.]

There was also an area of bone destruction extending from the right lower canine to the left lower second premolar with a few sclerotic patches (fig. 2).

The enlarged right maxilla and malar bone gave a picture of diffuse and fine-grained hyperostosis. There was some exophthalmos of the right eye and a little ptosis on the same side (fig. 3a). Investigations showed blood cholesterol at the lower limit of normal and no diabetes insipidus, rendering a diagnosis of Schüller-Christian's disease unsuitable. Serum calcium lay within the upper limits of normal range; the blood-count was normal; there were no Bence-Jones proteoses in the urine; the Wassermann and Kahn reactions were negative; and radiographs of pelvis and long bones showed no abnormality. A biopsy from the right maxilla and the right side of the mandible showed the picture of osteitis fibrosa in each case. Dr. Laurent thought at one time that the case might be an early state of hyperparathyroidism; but the condition did not develop in that sense. When seen again in two years the bony protuberances had increased in size, especially that at the right mandibular angle, and the proptosis had increased (fig. 3b). The latter was apparently due to the formation of a boss of bone under the right eye. The serum calcium was then 10.9 mg. per 100 ml. It was decided to reduce the mandibular prominence for cosmetic reasons and this was done by Commander J. M. Banks and Mr. F. A. Walker (fig. 3c). The bone was found to be of leathery consistency. Professor W. D. Newcombe reported on the material removed as follows: "All the material is substantially the same, viz. osteitis fibrosa. The histology has changed considerably in the last two years, and now it is much more active with much woven bone formation and many spindle cells with very delicate collagen. If this type of alteration progresses much further the condition will become sarcomatous."

CASE II.—A married woman of 25 complained of swellings of the jaws. Abnormal thickness of the lower jaw on the right side was first noticed six years ago by a dental surgeon, and radiographs had since been taken and a diagnosis of adamantinoma made. There had never been any pain, redness, or discharge, and general health was excellent. Wassermann and Kahn reactions were negative. She had recently noticed new swellings on the left side of both jaws.

(6) *Malignant disease, i.e. post-radium necrosis.*—Radium necrosis is becoming very much less common with the advances in therapy. There is little that one can do in these cases in the way of any extensive treatment. The necrosis is slow and there is a reluctance to interfere. The deciding factor is the prognosis of the case. If this is poor then the best line of treatment is purely palliative, on the other hand with a younger patient with a good prognosis one might be tempted to greater efforts.

I think it is a little premature to lay down hard and fast rules regarding the optimum doses of penicillin, perhaps further work will strengthen our position.

My thanks are due to Professor Kilner, Messrs. R. P. Osborne and J. P. Reidy, and Mr. J. W. Hallam for permission to include some of their cases. My grateful thanks are due to Professor McIntosh and his staff and also to the radiologists to Stoke Mandeville and the Middlesex Hospitals, and to Professor Windeyer for his case treated by radiotherapy; I must also thank the Director-General of Medical Services of the Ministry of Pensions for permission to publish this Paper.

REFERENCES

1 Hudson, R. Vaughan (1946) *Proc. R. Soc. Med.*, 39, 371.
2 Butler, E. C. B. (1946) *Proc. R. Soc. Med.*, 39, 379.
3 Mowlem, Rainsford (1944) *Brit. med. J.* (i), 517.
4 Henry, T. Cradock (1946) *Brit. Dent. J.*, 81, 275.
5 Walker, D. Greer (1945) *Proc. R. Soc. Med.*, 38, 451.
6 MacGregor, A. B. (1945) *Proc. R. Soc. Med.*, 38, 639.

Regional Osteitis Fibrosa Affecting the Facial Bones: Two Cases

By Martin A. Rushton, M.D., L.D.S.

Many conditions differing in various ways have been grouped under the names osteitis fibrosa, osteodystrophia fibrosa, &c., on the grounds of their histological appearances.

A type quite commonly found in the jaws and in which there is no evidence of hyperparathyroidism has been called local or focal osteitis fibrosa, ossifying fibroma, and other names. This variety usually affects one bone only and often only one part of it. Occasionally cases occur in which there is the same type of lesion confined to the facial or cranial bones but affecting several of them. The lesion is, however, not symmetrical as it is in the classical descriptions of leontiasis ossea. Such cases may conveniently be called the regional type of osteitis fibrosa since there is in them no evidence of disturbance beyond the head region.

In the two cases to be described the lesions, chiefly of the hyperostotic-porotic variety, were first noticed towards the end of the second decade, were asymmetrical, progressive, and not associated with any observed blood changes, except a raised alkaline plasma phosphatase.

I report the first case by the kindness of my colleague, Mr. F. A. Walker.

Case I.—A soldier of 21 had noticed a lump on the right side of the lower jaw growing slowly for four or five years. There were no other symptoms. On examination it was found that the mandible was much enlarged in the region of the right angle and somewhat also around the symphysis. The right maxilla and malar bone were also much enlarged. Radiographs showed an area of bone rarefaction from the right lower first molar region to the condylar neck, with hyperostosis of a porotic kind (fig. 1).

Section of Otology

President—H. V. Forster, M.C., M.B., Ch.B., M.Sc.

[*December* 6, 1946]

Technique of Fenestration Operation.

Mr. E. R. Garnett Passe showed a coloured film of the fenestration operation performed through the endaural approach. In this operation a cartilage stopple was inserted. Illustrations were also shown of the new fenestra without the cartilage stopple insertion (*vide infra*). Mr. Passe said that he had used a cartilage stopple insertion in over 100 cases and that he had never obtained more than 40 to 45 decibel improvement; whereas in a further series of 70 cases, in which he has used his modified fenestra without the stopple insertion he has obtained as much as an initial 60 decibel improvement in two of his cases. He said that the cartilage stopple insertion was a technique he had learned from Dr. Lempert of New York, but he had given up the cartilage stopple insertion for the following reasons: (1) The cartilage stopple does not permit as great an increase in hearing acuity. (2) It does not materially reduce post-operative serous labyrinthitis. (3) It does not necessarily prevent bony or fibrous closure of the fenestra. (4) There is the further difficulty of insertion and the added risk that the membranous labyrinth might be injured during its insertion and associated manipulation.

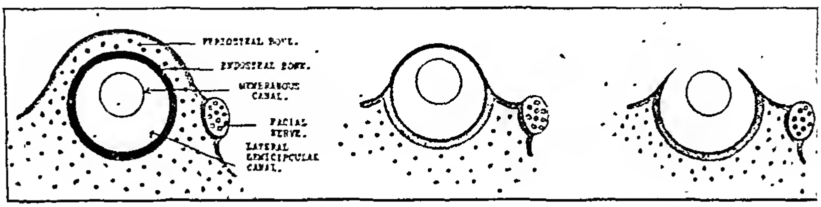


Fig. 1. Fig. 2. Fig. 3.

Fig. 1.—Cross section of lateral semicircular canal. Fig. 2.—Periosteal bone removed down to endosteal bone over a large area. Fig. 3.—Endosteal bone thinned down until the roof is finally removed.

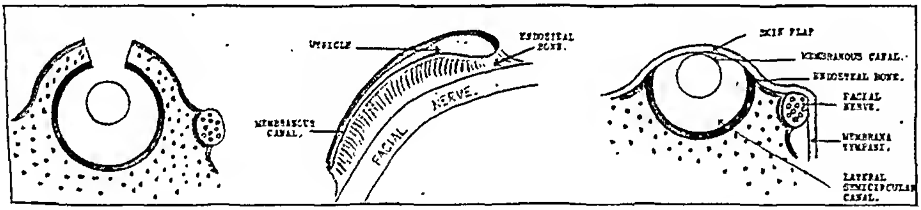


Fig. 4. Fig. 5. Fig. 6.

Fig. 4.—The old type of fenestra made for use with the cartilage stopple. Fig. 5.—Lateral view of the fenestra in roof of vestibule and canal showing fenestra seated on top of a ridge. Fig. 6.—Skin flap in situ. Note that it is in contact with the membranous canal.

However, he felt that the film would give a good idea of the technique performed in the fenestration operation. The film showed the various stages of the operation carried out under pentothal anæsthesia together with the first dressing, also under pentothal anæsthesia, six days later.

Bilateral Clinical Otosclerosis Treated By the Fenestration Operation Using the Cartilage Stopple and the Endaural Approach.—E. R. Garnett Passe, F.R.C.S.

History.—J. B. McG., aged 34. Increasing bilateral deafness and tinnitus. Deafness commenced at the age of 28 associated with high pitched severe tinnitus. Marked family history of deafness.

On examination.—Clinical and audiometric examination revealed him to be a case of clinical otosclerosis.

Operation (January 18, 1946).—Endaural incision, mastoid cavity excavated.

On examination the thickness of the lower jaw was found to be abnormally great especially at its anterior part on the right (fig. 4a). The alveolar process of the left maxilla was also very much thickened. There were visible veins running vertically in the skin beneath the chin (fig. 4b). The occlusion of the anterior teeth was abnormal and according to the patient was not formerly so (fig. 4c). Mucous membrane was normal. Radiographs showed that almost the whole mandible was affected by osteitis fibrosa of a hyperostotic-porotic type but with occasional patches of sclerosis (fig. 5). The texture of the bone was a very fine stippling, with occasional areas of almost complete bone absorption and with a thin but unbroken cortex. The alveolar and palatine parts of the left maxilla were affected in the same manner, the abnormal bone ceasing sharply at the mid-line (fig. 6).

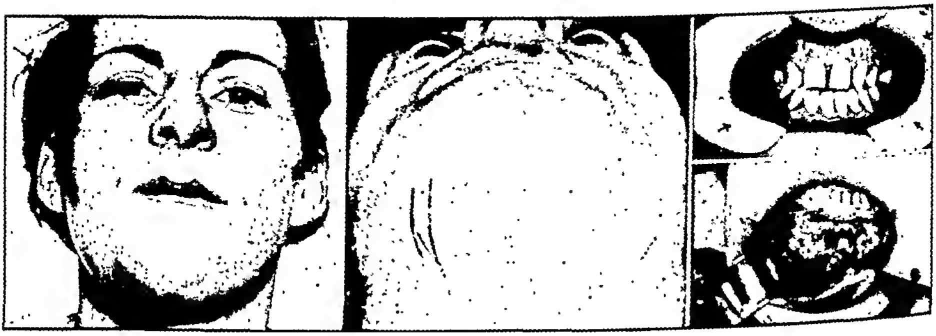

(a) (b) (c)

FIG. 4.

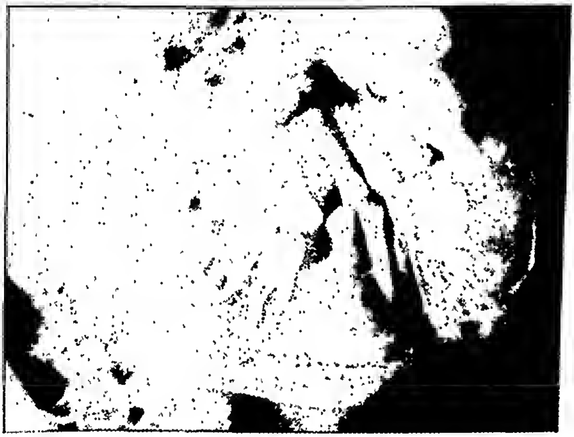


FIG. 5.

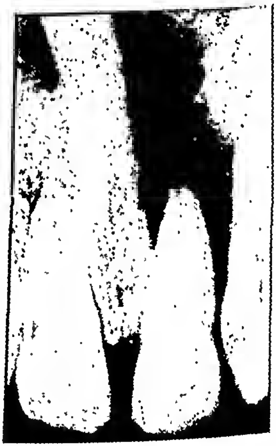


FIG. 6.

CASE II. [Figs. 4, 5, 6.]

The left malar bone seemed porotic compared with the right but was not clinically enlarged. There appeared also to be an area of porosis on the right side of the cranial vault, the size of two shillings, but again there was no clinical enlargement. Radiographs of the pelvis and right femur showed no abnormality; the serum calcium was 10·9 mg. per 100 ml.; and the plasma alkaline phosphatase was 45 phenol units.

On the advice of Dr. Levitt the patient was treated by radiotherapy preparatory to a cosmetic reduction of the bony prominences. The latter was performed five months later (Sir Harold Gillies and M. A. R.), a large section of the outer side of the lower jaw from molar region to molar region being removed and the prominence of the maxilla being sliced off. Sections of the tissue removed showed the same appearance in each jaw. All cortical bone was being actively absorbed, with large numbers of giant-cell osteoclasts, including the cortical bone around the mandibular canal, and the whole inner part of the bone had come to consist of a fine connective tissue containing innumerable small bone nodules of inactive appearance.. A certain amount of new subperiosteal and other bone was being formed. The lower left canine tooth, which had to be extracted, showed no abnormalities of structure and, in particular, normal cementum.

We found ourselves quite unable to offer any prognosis for these cases or to devise any useful treatment other than a palliative cosmetic procedure.

I am indebted to Sir Harold Gillies for allowing me to describe these cases from the Plastic and Jaw Unit E.M.S., Basingstoke.

Section of Otology

President—H. V. Forster, M.C., M.B., Ch.B., M.Sc.

[*December* 6, 1946]

Technique of Fenestration Operation.

Mr. E. R. Garnett Passe showed a coloured film of the fenestration operation performed through the endaural approach. In this operation a cartilage stopple was inserted. Illustrations were also shown of the new fenestra without the cartilage stopple insertion (*vide infra*). Mr. Passe said that he had used a cartilage stopple insertion in over 100 cases and that he had never obtained more than 40 to 45 decibel improvement; whereas in a further series of 70 cases, in which he has used his modified fenestra without the stopple insertion he has obtained as much as an initial 60 decibel improvement in two of his cases. He said that the cartilage stopple insertion was a technique he had learned from Dr. Lempert of New York, but he had given up the cartilage stopple insertion for the following reasons: (1) The cartilage stopple does not permit as great an increase in hearing acuity. (2) It does not materially reduce post-operative serous labyrinthitis. (3) It does not necessarily prevent bony or fibrous closure of the fenestra. (4) There is the further difficulty of insertion and the added risk that the membranous labyrinth might be injured during its insertion and associated manipulation.

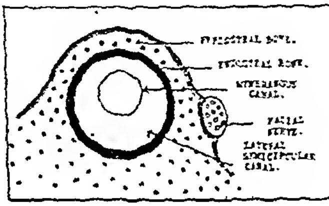


Fig. 1.

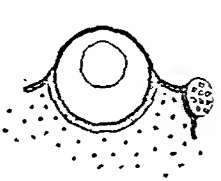


Fig. 2.

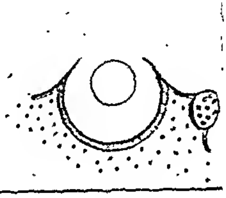


Fig. 3.

Fig. 1.—Cross section of lateral semicircular canal. Fig. 2.—Periosteal bone removed down to endosteal bone over a large area. *Fig. 3.*—Endosteal bone thinned down until the roof is finally removed.

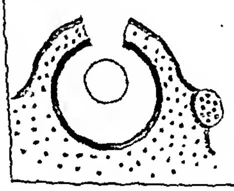


Fig. 4.

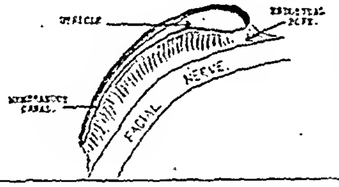


Fig. 5.

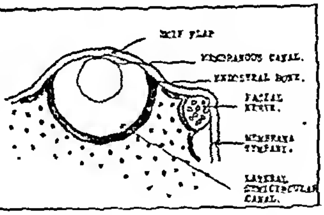


Fig. 6.

Fig. 4.—The old type of fenestra made for use with the cartilage stopple. Fig. 5.—Lateral view of the fenestra in roof of vestibule and canal showing fenestra seated on top of a ridge. Fig. 6.—Skin flap in situ. Note that it is in contact with the membranous canal.

However, he felt that the film would give a good idea of the technique performed in the fenestration operation. The film showed the various stages of the operation carried out under pentothal anæsthesia together with the first dressing, also under pentothal anæsthesia, six days later.

Bilateral Clinical Otosclerosis Treated By the Fenestration Operation Using the Cartilage Stopple and the Endaural Approach.—E. R. Garnett Passe, F.R.C.S.

History.—J. B. McG., aged 34. Increasing bilateral deafness and tinnitus. Deafness commenced at the age of 28 associated with high pitched severe tinnitus. Marked family history of deafness.

On examination.—Clinical and audiometric examination revealed him to be a case of clinical otosclerosis.

Operation (January 18, 1946).—Endaural incision, mastoid cavity excavated.

Membrano-cutaneous flap fashioned, fenestration performed over vestibule and ampulla of lateral canal. Cartilage stopple fashioned from spine of the helix and inserted into fenestra. Jacobson's nerve on promontory destroyed by diathermy.

Cavity was completely healed within five weeks. Patient left hospital on twelfth day, and was able to play golf four weeks from the day of the operation.

Frequency (d.v.)	128	256	512	1024	2048	4096
Hearing before operation (decibels)	60	60	60	55	45	40
Hearing eleven months after operation (decibels)	35	30	30	35	25	15

His hearing has reached a satisfactory level of practical conversational value, and he now has no difficulty in hearing at his work as a draughtsman, or in his social life. To date there is no tinnitus in the operated ear.

An Operating Microscope for the Fenestration Operation.—J. F. SIMPSON, F.R.C.S.

Mr. Simpson said that he had brought this to the notice of the Section in order that members might have an opportunity of seeing an operating microscope which could actually be obtained in this country. It was made by Baker in Holborn. All that he had done was to have a prismatic attachment instead of a mirror or a direct light screwed on to the microscope itself. It had a useful magnification with the three sets of eyepieces—3, 7, and 10·5. The working distance was 130 mm.

Asked by Mr. Simson Hall what was the working distance at the highest magnification, he replied that it was very little different.

Review of Surgery of Otosclerosis

By TERENCE CAWTHORNE, F.R.C.S.

IT was in 1841 that Toynbee firmly established the connexion between deafness and ankylosis of the footplate of the stapes. In the previous century Morgagni, Meckel and Valsalva (quoted by Nager, *1928*) had all suspected that ankylosis of the stapes footplate might be responsible for certain forms of deafness, but it was Toynbee's work, which he continued to develop after his original publication, that really drew the attention of otologists to the condition that we know as otosclerosis, particularly when he stressed that, so far as his investigations took him, the organ of hearing itself was intact. It was this that made otologists realize that the one hope of a cure lay in overcoming the bony barrier that held back the sound waves from reaching the apparently normal cochlea. It is interesting to note that as recently as 1944, in a very fine paper on otosclerosis, Guild also remarked on the absence of any internal ear changes in a series of otosclerotic temporal bones.

In 1876, Kessel described a series of cases in which he removed the stapes. This procedure was tried by many and a Boston surgeon—Jack, 1894—described fifty such cases. There were, however, certain rather serious drawbacks to it; namely that the crura easily broke off leaving the footplate firmly fixed in the oval window and, where it was possible to remove the stapes, suppuration not infrequently supervened, giving rise at the best to a dead cochlea and, at the worst, to a dead patient.

In 1897 Passow, and in 1899 Floderus, described an operation in which they trephined an opening into the promontory, covering it with a mucoperiosteal flap. Like removal of the stapes, this operation soon fell into disrepute because it never resulted in lasting improvement and often made the patient worse. Thus it was clear to otologists at that time that the cochlear approach was not feasible and it was abandoned.

It was not until *1911* that *Bárány*, the Hungarian otologist, conceived the idea of decompressing the vestibular part of the labyrinth in the hope that, by reducing the perilymph pressure, more freedom of movement would be permitted to the already restricted stapes; he selected the posterior semicircular canal for this. In 1913, Jenkins, my predecessor at King's College Hospital, described before the International Medical Congress in London two cases in which he had made an opening in the external semicircular canal. At that time he thought that one of the contributing factors in otosclerosis might be an alteration in either the physical or chemical properties of the labyrinthine fluids, and he hoped that, by tapping the encased perilymph, the fluid might return to normal and some improvement in hearing might result. I was never fortunate enough to see him doing any of this work, but I understand from Mr. W. Wilson that any improvement so brought about was only fleeting.

During the early part of the first World War Bárány was serving with the Austrian Army and was captured by the Russians. As a Nobel Prize winner he was allowed, through the good offices of the International Red Cross, to go to a neutral country—Sweden—where he continued his work. There he attracted the attention of the Swedish otologist—Holmgren—who, in 1917, continuing on the same lines, and believing that decompression of the perilymph space was the answer to the problem, chose the superior semicircular canal, his object being to make an opening at its upper surface so that the dura might fall back on the top of the opening, thus delaying any bony closure. It is interesting to note that, within a matter of four or five years, three different otologists from three different countries each chose a different semicircular canal for his attack.

Holmgren soon abandoned the superior canal and turned his attention back to the lateral canal and even to the promontory, and, in 1921, he was trephining the promontory, fashioning the mucoperiosteal flap, using magnifying spectacles and a binocular dissecting microscope.

This work attracted the attention of a French otologist, Sourdille of Nantes, who visited Bárány and Holmgren in 1924 and was deeply impressed by the work they were doing. He decided that he must do this kind of work himself, but he soon started to think along somewhat different lines. He felt that the key to the problem lay in making and maintaining an opening into the perilymph space in such a manner that airborne sound waves could reach and be transmitted to the labyrinthine fluids. He felt that the best way of achieving this was to cover the fistula made in the lateral canal with a mucocutaneous flap continuous with the tympanic membrane. This, of course, meant an open operation and, in 1929, he described his operation of tympanopexy (Sourdille, 1932). It was an open operation done in two, three, or even four stages, these multiple stages being found necessary to avoid or combat infection. Although I have heard him describe his operation, I never had the opportunity of seeing him do it, but from the descriptions of the operation it was apparent that this was far from being a simple procedure.

During this time Holmgren, too, did some open operations, though on the whole he preferred the closed operation from behind the ear leaving the tympanum and attic intact; particular attention being devoted to preventing the fenestra from closing. In 1938, Mr. Macbeth and I had the privilege of spending several days with Holmgren and we were able to see him do several operations. He then was using radon emanations to discourage the regrowth of bone over the fistula.

In 1938 Lempert of New York described a one-stage open operation in which the approach was made through the meatus and which was similar in principle to that of Sourdille. It was done in one stage instead of in three, and the endaural approach seemed to cause less reaction and the incidence of infection and other complications was slight. In 1940 and 1941 he described further modifications of his endaural fenestration. He had at first continued rather on the same lines as Sourdille, removing the head of the malleus and leaving the incus intact, but later he removed the incus as well, and brought the fenestra farther forward until it was what he termed *fenestra nov-ovalis*, lying in the dome of the vestibule and including a part of the ampulla just above the oval window and separated from it by the facial canal. He brought this fenestra farther forward for two main reasons:—firstly because, as he said, new bone formation was rarely found in that part of the capsule of the labyrinth, and secondly, because the bringing forward of the fenestra enabled it to be covered by mucous-membrane-lined Shrapnell's membrane instead of by the mucoperiosteal-lined membrane of the posterior meatal wall which was necessary when the fenestra was more posteriorly placed. He felt that in this way there was less chance of the fenestra closing up with bone. About this time he also described the insertion of a little metal obturator in the hope of keeping the fenestra open.

In 1945 Lempert again published his results with what he termed a mobile cartilaginous stopple: a small piece of cartilage suitably shaped and taken from one of the auricular cartilages which was placed within the fenestra and was covered with the usual tympano-meatal flap. In this connexion you may be interested to know that when I was in America last summer Lempert was not using a stopple. He said that, though he had not been using it recently, it was quite possible that he might return to it later on. I found that several other workers had also abandoned the stopple.

Shambaugh of Chicago in 1942 published an article in the *Journal of the American Medical Association* in which he described the Lempert technique but adding to it constant irrigation and the use of a binocular dissecting microscope. In July 1946 in the *Archives of Otolaryngology* he described in detail certain variations, or perhaps I should say, additions to the Lempert procedure for which he claimed better results. The removal of much periosteal bone from the canal around the fistula, the avoidance of splintering of the endosteal bone, having the bridge of membrane between the drum and the fenestra as short and as mobile as possible, sponge dressings for the cavity, and special positioning of the head during the early post-operative period, were some of the details on which he placed emphasis.

In the evolution of this operation to its present stage there are three names which stand out—Holmgren, Sourdille and Lempert; Holmgren for his enthusiasm, and for his patience and perseverance, and, particularly, for the value of his example in interesting others in this work at a time when surgical treatment was in disfavour; Sourdille, who deserves great credit for designing an open operation that allowed airborne sound waves to be transmitted directly to the labyrinthine fluids; finally, Lempert, whose superb technique and endaural approach have simplified and perfected the open operation and have made it so safe that now this procedure can be carried out without any danger to life and with negligible risk of infection. His one-stage procedure is really a simplication of Sourdille's operation and the principle remains the same, namely, to quote Lempert's own words, "to mobilize the perilymph and endolymphatic fluids".

It is of interest to recall that, in this country, in addition to the work of Jenkins already mentioned, Kisch, before the First World War, operated on a series of cases of otosclerosis, trephining the promontory and covering the fistula with a periosteal flap. Hutchinson described his experiences with Sourdille's operation before this Section in 1936; Howarth in 1937 gave an account of his experience of the Holmgren type of operation; and in 1939 Passe described a series of cases in which he had carried out a fenestration operation; in 1944 Simson Hall, before this Section, gave an account of his experiences with the fenestration operation over a period of six years.

Towards the end of 1945, not being at all satisfied with my own results from fenestration, I decided to revert to the earlier procedure of removing the stapes; this was done in some twenty cases. Some of the difficulties that had formerly been noted were encountered; one of them being that the crura broke off with great ease, leaving the footplate fixed in the oval window. It was, however, quite easy to break through the footplate, but not always easy, even with ample magnification, to remove the pieces as the footplate usually fragmented inwards, the pieces adhering to the rim of the oval window. The results were variable, but on the whole disappointing, though I am not sure that this route may not in the end give good results. After seeing the work of Lempert, Shambaugh, Sullivan and Walsh and hearing of the experiences of other otologists during a visit to America in the summer of 1946, I decided to return to the fenestration operation. I have found that, no matter how carefully an operation is described nor how detailed are the illustrations of the various steps, it has been very easy for me at any rate to overlook certain minutiæ of technique that, in an operation such as fenestration, may count for so much.

This leads to the next part of this review, namely, the two factors essential for success in this operation. The first is complete familiarity with the procedure—familiarity not only from reading the descriptions but also familiarity from having done many operations on the temporal bone, on the cadaver and also of course of having seen an expert do the operation. My own experience has been that, although I was not unfamiliar with operations on the labyrinth, it was not until I had actually seen a number of fenestrations, through the kindness of my American and Canadian friends, that I was able to appreciate certain little technical manœuvres, particularly in connexion with the formation of the flap, which were very important and I realized that it was quite impossible for me to pick up everything from articles. In addition to work on the temporal bone and cadaver, and seeing other people perform the operation, it is important to gain familiarity in making the flap by using this approach for modified radical and certain radical mastoid operations. It is also advisable to take advantage of any case of labyrinthectomy for Ménière's disease to improve technique in making the fenestra.

There are two small details concerning the operation that deserve special mention: The first is magnification. In order properly to carry out this operation, and this applies particularly to the making and finishing off of the fenestra, it is necessary to work in a magnified field. Holmgren was the first to advocate the use of a binocular dissecting microscope giving ten diameters of magnification, but later contented himself with Zeiss-Ullstrom glasses giving two diameters of magnification. Lempert himself does not use a microscope for the operation and is able to do the most delicate work using only two diameter glasses. I do not however think that there are many people with eyes like his and most workers prefer a higher degree of magnification for the actual fenestration. I have been accustomed for some years to use a Leitz dissecting microscope giving ten diameters of magnification, and having a working distance of 22 cm. (Cawthorne, 1941) for all operations on the labyrinth and facial nerve, and I would not consider undertaking a fenestration without it.

The other detail that I think deserves special mention is the amount of time to be devoted to these operations. They should not be done as part of a routine list. Each takes from one and a half to three or more hours according to the difficulties of the operation and the experience of the surgeon, but the time factor should not be considered when embarking on them and I think that they should be done at a special session. Many surgeons prefer to do only one at a time, but it is possible for some surgeons to do two or even more in one session.

The next factor that requires consideration is the proper selection of cases. This is not an easy matter and each surgeon must, to a certain extent, form his own standards by which to select cases suitable for operation. An added difficulty in selection is that practically every patient who comes up for consideration is eager to have the operation. Most of them have heard of good results, or have read in the lay press glowing accounts of what can be expected. It is therefore of considerable importance at the very outset to be as objective as possible in the selection of cases and to be quite frank with those patients for whom an operation seems unsuitable. In their eagerness to have the operation some patients will even go to the extent of trying to deceive the examiner; sometimes they become very of the labyrinth, and secondly, because the bringing forward of the fenestra enabled it to be covered by mucous-membrane-lined Shrapnell's membrane instead of by the mucoperiosteal-lined membrane of the posterior meatal wall which was necessary when the fenestra was more posteriorly placed. He felt that in this way there was less chance of the fenestra closing up with bone. About this time he also described the insertion of a little metal obturator in the hope of keeping the fenestra open.

In 1945 Lempert again published his results with what he termed a mobile cartilaginous stopple: a small piece of cartilage suitably shaped and taken from one of the auricular cartilages which was placed within the fenestra and was covered with the usual tympano-meatal flap. In this connexion you may be interested to know that when I was in America last summer Lempert was not using a stopple. He said that, though he had not been using it recently, it was quite possible that he might return to it later on. I found that several other workers had also abandoned the stopple.

Shambaugh of Chicago in 1942 published an article in the *Journal of the American Medical Association* in which he described the Lempert technique but adding to it constant irrigation and the use of a binocular dissecting microscope. In July 1946 in the *Archives of Otolaryngology* he described in detail certain variations, or perhaps I should say, additions to the Lempert procedure for which he claimed better results. The removal of much periosteal bone from the canal around the fistula, the avoidance of splintering of the endosteal bone, having the bridge of membrane between the drum and the fenestra as short and as mobile as possible, sponge dressings for the cavity, and special positioning of the head during the early post-operative period, were some of the details on which he placed emphasis.

In the evolution of this operation to its present stage there are three names which stand out—Holmgren, Sourdille and Lempert; Holmgren for his enthusiasm, and for his patience and perseverance, and, particularly, for the value of his example in interesting others in this work at a time when surgical treatment was in disfavour; Sourdille, who deserves great credit for designing an open operation that allowed airborne sound waves to be transmitted directly to the labyrinthine fluids; finally, Lempert, whose superb technique and endaural approach have simplified and perfected the open operation and have made it so safe that now this procedure can be carried out without any danger to life and with negligible risk of infection. His one-stage procedure is really a simplication of Sourdille's operation and the principle remains the same, namely, to quote Lempert's own words, "to mobilize the perilymph and endolymphatic fluids".

It is of interest to recall that, in this country, in addition to the work of Jenkins already mentioned, Kisch, before the First World War, operated on a series of cases of otosclerosis, trephining the promontory and covering the fistula with a periosteal flap. Hutchinson described his experiences with Sourdille's operation before this Section in 1936; Howarth in 1937 gave an account of his experience of the Holmgren type of operation; and in 1939 Passe described a series of cases in which he had carried out a fenestration operation; in 1944 Simson Hall, before this Section, gave an account of his experiences with the fenestration operation over a period of six years.

Towards the end of 1945, not being at all satisfied with my own results from fenestration, I decided to revert to the earlier procedure of removing the stapes; this was done in some twenty cases. Some of the difficulties that had formerly been noted were encountered; one of them being that the crura broke off with great ease, leaving the footplate fixed in the oval window. It was, however, quite easy to break through the footplate, but not always easy, even with ample magnification, to remove the pieces as the footplate usually fragmented inwards, the pieces adhering to the rim of the oval window. The results were variable, but on the whole disappointing, though I am not sure that this route may not in the end give able to hear as well in a noise. This is perhaps the most significant and striking sign of all and I would say that the disappearance of paracusis is a definite contra-indication to operation.

(4) *Bone conduction.*—It is known that deafness due to internal ear changes is always accompanied by loss of acuity for bone-conducted sound and such loss has been generally accepted as evidence of perceptive (inner ear or nerve) deafness. There is, however, a group of cases in which loss of bone conduction is a prominent feature, but none of the other stigmata of perceptive deafness already mentioned are seen. It is therefore not beyond the bounds of possibility that shortened bone conduction can result from conditions other than perceptive deafness. It has been suggested that involvement of both round and oval windows by otosclerotic bone may produce this phenomenon and in favour of this is the fact that the rapidly advancing cases of otosclerosis which exhibit the flamingo-tinged drum often have loss of bone conduction without any other signs of perceptive deafness and it is in just these cases that the otosclerotic bone spreads widely and rapidly. Whilst very much shortened bone conduction usually means perceptive deafness, minor losses, particularly if they are unaccompanied by any other signs of perceptive deafness, may, in some instances, be due to other factors. With regard to the method of estimating the acuity of hearing for bone-conducted sound, this still presents certain difficulties. Bone-conduction receivers used in connexion with a pure tone audiometer do not give results that are in any way comparable as regards accuracy with air-conduction figures. For this reason it is, I feel, wiser not to put air and bone conduction results on the same chart because by doing so it may be inferred that they are of comparable accuracy. Many otologists still prefer to use the tuning fork and for those that do this it is wise to use the tuning forks of the three critical speech frequencies (512, 1024, 2048 d.v.). However, no matter how carefully they are carried out, bone-conduction tests are merely approximate and should not be regarded as anything else.

With regard to the quantitative aspect of deafness, it is necessary to have some idea of the amount of improvement that can be expected. It has been estimated that, in good cases, an improvement of 25 decibels can be expected for the critical speech frequencies. Bearing in mind that for these frequencies a hearing loss greater than 30 decibels reduces the hearing for speech to less than three feet it can be said that the best results as regards practical hearing for speech will follow where the pre-operative hearing loss for the critical speech frequencies has not fallen below 50 decibels. Of course whilst hearing for speech is the one thing above all that the deaf patient desires, an operation need not necessarily be ruled out because the hearing after operation is unlikely to reach the 30 decibel level. It is, however, important to give the patient some idea of how much improvement he can expect and the figures just mentioned form a useful guide.

A good functional result from fenestration can only be assured by careful judgment in the selection of the case and scrupulous attention to an admittedly difficult technique. If both these essential requirements are satisfied then it is reasonable to anticipate an improvement in hearing in about 75% of the cases operated upon. Of these, however, one-third will either have such a small improvement that it is not of any practical value, or the hearing will within a few months of the operation return slowly or quickly to its former level. Hence it may be said that, given favourable conditions, there is a 50% chance of a substantial improvement being maintained for a number of years. Exactly how long an improvement can last is not known, but it is generally estimated that if the initial improvement is sustained for more than six months it may last for several years. Nevertheless, most observers are in favour of waiting for two years before declaring that an improvement is worthy of being put on record. Of the remain-expert at this as not infrequently they have been through one or more special otological examinations before they finally appear as candidates for operation. I saw Lempert examine a series of cases and I was very impressed with the careful way in which he carried out the routine speech and tuning-fork tests. I noted that in several cases he tested the accuracy of the patient's replies by surreptitiously damping a struck tuning fork before applying it to the patient's ears or skull. On questioning him about this procedure he said that all his patients had already undergone several otological examinations and they were all trying to persuade him to do the operation, even though not a few were unsuitable subjects.

With regard to the type of case which is suitable for operation, I think it may be safely said that any case of uncomplicated otosclerosis whose hearing loss is not greater than 55 decibels for the critical speech frequencies (512, 1024, 2048 d.v.) is suitable for operation. There are, of course, a variety of conditions and cases of otosclerosis complicated by other conditions which may be said to hover on the border-line of suitability. Experience has, however, shown that the cases already mentioned as being suitable are the ones most likely to give consistently good results. It is generally agreed that this operation should be limited to cases of otosclerosis with normal tympanic membranes. It has been tried on cases where the deafness is thought to be due to intratympanic adhesions binding down the membrane and ossicular chain but, if we accept the principle that improvement in hearing is caused by movements of an unimpeded tympanic membrane being transmitted through a flap over the fenestra which is continuous with the tympanic membrane, then, clearly, good results can only come if the tympanic membrane is free to move. Generally speaking the selection of cases for operation may be considered under the qualitative and quantitative aspects of the deafness.

As regards the qualitative aspect of the deafness, it is well known and generally accepted that if the operation is to be successful the organ of hearing itself must be able, without difficulty or discomfort, to appreciate the increased sounds that a fenestration will bring to it. No matter how perfect the fenestration operation is, nor how patent the fenestra is maintained, little or no benefit will accrue if the organ of hearing itself is unable properly to perceive the sounds that are brought to it. There are certain criteria with which we are all familiar and by which we can tell when a patient with otosclerosis also has internal ear changes. The most significant are alteration in the timbre of the voice, intolerance of amplification, the disappearance of paracusis, and loss of ability to perceive bone-conducted sounds.

(1) *Alteration in the timbre of the voice.*—Patients whose deafness is of the conductive type only have, of course, soft speaking voices. Any noticeable increase in the loudness of the voice, particularly if it does not appear to be very well regulated and has a somewhat hollow sound, suggests internal ear changes that are preventing the patient from hearing his own voice properly. This should always be regarded as a bad sign so far as operation is concerned.

(2) *Intolerance of amplification.*—The patient with severe conductive deafness, as in otosclerosis, is usually able to tolerate amplified speech and often hears particularly well on the telephone or with a hearing aid. Any noticeable internal ear changes will reduce this tolerance of amplification as in such cases the margin between hearing and discomfort is reduced. It is for this reason that any intolerance of amplification should be looked upon as being an unfavourable sign because even if the fenestration were successful the patient might find the impact of unimpeded sound upon his defective cochlea unbearable.

(3) *Disappearance of paracusis.*—Nearly every patient with otosclerosis is able to hear better in noisy surroundings and it will be found that, in the more advanced cases where there are obvious signs of internal ear changes, the patient is no longer

able to hear as well in a noise. This is perhaps the most significant and sinister sign of all and I would say that the disappearance of paracusis is a definite contra-indication to operation.

(4) *Bone conduction.*—It is known that deafness due to internal ear changes is always accompanied by loss of acuity for bone-conducted sound and such loss has been generally accepted as evidence of perceptive (inner ear or nerve) deafness. There is, however, a group of cases in which loss of bone conduction is a prominent feature, but none of the other stigmata of perceptive deafness already mentioned are seen. It is therefore not beyond the bounds of possibility that shortened bone conduction can result from conditions other than perceptive deafness. It has been suggested that involvement of both round and oval windows by otosclerotic bone may produce this phenomenon and in favour of this is the fact that the rapidly advancing cases of otosclerosis which exhibit the flamingo-tinged drum often have loss of bone conduction without any other signs of perceptive deafness and it is in just these cases that the otosclerotic bone spreads widely and rapidly. Whilst very much shortened bone conduction usually means perceptive deafness, minor losses, particularly if they are unaccompanied by any other signs of perceptive deafness, may, in some instances, be due to other factors. With regard to the method of estimating the acuity of hearing for bone-conducted sound, this still presents certain difficulties. Bone-conduction receivers used in connexion with a pure tone audiometer do not give results that are in any way comparable as regards accuracy with air-conduction figures. For this reason it is, I feel, wiser not to put air and bone conduction results on the same chart because by doing so it may be inferred that they are of comparable accuracy. Many otologists still prefer to use the tuning fork and for those that do this it is wise to use the tuning forks of the three critical speech frequencies (512, 1024, 2048 d.v.). However, no matter how carefully they are carried out, bone-conduction tests are merely approximate and should not be regarded as anything else.

With regard to the quantitative aspect of deafness, it is necessary to have some idea of the amount of improvement that can be expected. It has been estimated that, in good cases, an improvement of 25 decibels can be expected for the critical speech frequencies. Bearing in mind that for these frequencies a hearing loss greater than 30 decibels reduces the hearing for speech to less than three feet it can be said that the best results as regards practical hearing for speech will follow where the pre-operative hearing loss for the critical speech frequencies has not fallen below 50 decibels. Of course whilst hearing for speech is the one thing above all that the deaf patient desires, an operation need not necessarily be ruled out because the hearing after operation is unlikely to reach the 30 decibel level. It is, however, important to give the patient some idea of how much improvement he can expect and the figures just mentioned form a useful guide.

A good functional result from fenestration can only be assured by careful judgment in the selection of the case and scrupulous attention to an admittedly difficult technique. If both these essential requirements are satisfied then it is reasonable to anticipate an improvement in hearing in about 75% of the cases operated upon. Of these, however, one-third will either have such a small improvement that it is not of any practical value, or the hearing will within a few months of the operation return slowly or quickly to its former level. Hence it may be said that, given favourable conditions, there is a 50% chance of a substantial improvement being maintained for a matter of years. Exactly how long an improvement can last is not known, but it is generally estimated that if the initial improvement is sustained for more than six months it may last for several years. Nevertheless, most observers are in favour of waiting for two years before declaring that an improvement is worthy of being put on record. Of the remain-expert at this as not infrequently they have been through one or more special otological examinations before they finally appear as candidates for operation. I saw Lempert examine a series of cases and I was very impressed with the careful way in which he carried out the routine speech and tuning-fork tests. I noted that in several cases he tested the accuracy of the patient's replies by surreptitiously damping a struck tuning fork before applying it to the patient's ears or skull. On questioning him about this procedure he said that all his patients had already undergone several otological examinations and they were all trying to persuade him to do the operation, even though not a few were unsuitable subjects.

With regard to the type of case which is suitable for operation, I think it may be safely said that any case of uncomplicated otosclerosis whose hearing loss is not greater than 55 decibels for the critical speech frequencies (512, 1024, 2048 d.v.) is suitable for operation. There are, of course, a variety of conditions and cases of otosclerosis complicated by other conditions which may be said to hover on the border-line of suitability. Experience has, however, shown that the cases already mentioned as being suitable are the ones most likely to give consistently good results. It is generally agreed that this operation should be limited to cases of otosclerosis with normal tympanic membranes. It has been tried on cases where the deafness is thought to be due to intratympanic adhesions binding down the membrane and ossicular chain but, if we accept the principle that improvement in hearing is caused by movements of an unimpeded tympanic membrane being transmitted through a flap over the fenestra which is continuous with the tympanic membrane, then, clearly, good results can only come if the tympanic membrane is free to move. Generally speaking the selection of cases for operation may be considered under the qualitative and quantitative aspects of the deafness.

As regards the qualitative aspect of the deafness, it is well known and generally accepted that if the operation is to be successful the organ of hearing itself must be able, without difficulty or discomfort, to appreciate the increased sounds that a fenestration will bring to it. No matter how perfect the fenestration operation is, nor how patent the fenestra is maintained, little or no benefit will accrue if the organ of hearing itself is unable properly to perceive the sounds that are brought to it. There are certain criteria with which we are all familiar and by which we can tell when a patient with otosclerosis also has internal ear changes. The most significant are alteration in the timbre of the voice, intolerance of amplification, the disappearance of paracusis, and loss of ability to perceive bone-conducted sounds.

(1) *Alteration in the timbre of the voice.*—Patients whose deafness is of the conductive type only have, of course, soft speaking voices. Any noticeable increase in the loudness of the voice, particularly if it does not appear to be very well regulated and has a somewhat hollow sound, suggests internal ear changes that are preventing the patient from hearing his own voice properly. This should always be regarded as a bad sign so far as operation is concerned.

(2) *Intolerance of amplification.*—The patient with severe conductive deafness, as in otosclerosis, is usually able to tolerate amplified speech and often hears particularly well on the telephone or with a hearing aid. Any noticeable internal ear changes will reduce this tolerance of amplification as in such cases the margin between hearing and discomfort is reduced. It is for this reason that any intolerance of amplification should be looked upon as being an unfavourable sign because even if the fenestration were successful the patient might find the impact of unimpeded sound upon his defective cochlea unbearable.

(3) *Disappearance of paracusis.*—Nearly every patient with otosclerosis is able to hear better in noisy surroundings and it will be found that, in the more advanced cases where there are obvious signs of internal ear changes, the patient is no longer

Mr. W. G. Scott-Brown reported a series of 24 recent cases in which a foreign body inlay was employed in an attempt to ensure that the new window remained patent. These prefabricated stopples are made from unplasticized methyl-methacrylate. They are prepared by turning them on a watchmaker's lathe with a tool which cuts them to the shape of a press-stud. They are made in three sizes, the smallest being 0·85 mm. in diameter, the next 0·95 mm. and the largest size 1·05 mm.

One of these inlays is gently pressed into the new window which has been prepared by the usual technique. The correct size can be felt to snap into position and can sometimes be heard to do so. It is fixed firmly into position, requiring quite an appreciable leverage to get it out again owing to the shape of the flange, but can be seen to move slightly up and down on touching it afterwards.

The usual technique is employed for cutting the tympano-meatal flap and turning it over the plastic inlay. Flavine and paraffin wool is used to pack on to the drum and flap and gives an easy and satisfactory springy pressure.

The cases were all operated on during the past year, and, though recent, demonstrate that a foreign body inlay can be safely used as there was no mortality, no infection around the inlay and no inlay has come out.

These early results show the hearing in only one case slightly worse than before operation, and all others improved, with several between 25 and 35 decibels gain in the conversational range.

(Three of the cases referred to in this series were shown.)

Mr. V. E. Negus said that he had been an onlooker in the evolution of the surgery of otosclerosis from its beginning. He had had the privilege of working with Mr. Jenkins and he had paid various visits to Professor Holmgren. He was in New York when the first presentation was given of Lempert's modification. He had nothing to add as to the technique of this operation but he wished to say that for many years he had had the pleasure of working with Mr. Cawthorne at King's College Hospital. He had seen his whole career from its beginning, and as he thought that it was always very important that there should be some concentration of work in one man's hands, he had devoted himself in other directions and had always handed over to Mr. Cawthorne in their partnership at King's College Hospital those cases which involved operations on the internal ear.

He thought that Mr. Cawthorne had given a masterly presentation of the subject that morning and in particular he commended his balanced judgment in the selection of cases. He had seen the care which he had taken for so many years in working through the different steps which he had described, from Ménière's disease to this operation, with eventual success. It might be taken as an example of the way to present a paper and also of the way to learn to treat patients. Mr. Cawthorne had added lustre to the Otological Department of King's College Hospital, which was founded by Urban Pritchard and carried on by Cheatle, Jenkins and Daggett.

Dr. I. Simson Hall said that he wished to touch upon several points which Mr. Cawthorne had raised. The microscope he considered to be essential to the highest quality of work. The optimum magnification was about 8, and the working distance should be at least sufficient to permit the end of the instrument used being passed underneath the objective without any danger of touching it, making a working distance of about 25 cm. in the average double nosepiece microscope desirable. An instrument with a single nosepiece gave closer working distance with equal facility, and it was becoming increasingly obvious that a microscope specially designed for this sort of work was necessary.

With regard to the stopple he said the decision regarding this means of keeping the fenestra open would have to be delayed because there was as yet no series of cases reported which had been done a sufficiently long time to warrant comparison with the older series done without a stopple. Up to six months ago in his hands the stopple appeared to be giving about 10% better results than a comparative series done without stopple; as, however, there were other factors to be considered such a figure could not be used as definite evidence.

In using a stopple Dr. Hall said that his method was to take the level of bone down until the canal was raised above the surface for, if possible, half its depth. The roof was then removed and the stopple therefore was raised some distance above the level of surrounding bone. It seems possible that good results might be obtained without the stopple by similar technique in which the overlying flap was placed in direct contact with the membranous labyrinth; it would thus be impossible for any growth or fibrosis to destroy the opening. He was experimenting with this particular method in suitable cases.

Dr. Hall agreed with Mr. Cawthorne in the importance of studying the patient's voice, and it was very frequently a useful factor in the selection of cases. This of course was also usually connected with the presence or absence of paracusis, and Dr. Hall said that the presence of paracusis was of importance, and if paracusis was found to have disappeared that fact also was of the greatest value as it was unlikely that fenestration would then be successful.

ing 25%, 20% will have little or no improvement, whilst in 5% the hearing in the operated ear may be made worse and, very occasionally, may disappear entirely. For this reason the worse hearing ear is usually to be preferred for operation.

With regard to the amount of improvement that can be expected: In good cases the average improvement for the critical speech frequencies is in the region of 25 decibels, but greater improvement, particularly for isolated frequencies in the lower tones, has been noted. It is interesting to find that much improvement in the frequencies above 2000 is not common. It is important that prospective patients should always realize that the amount of improvement is usually limited to the figures that have been quoted.

With regard to complications of the operation, fortunately the mortality is negligible and most of the fatalities reported have been due to cardiac failure. As this is an open operation there is bound to be a small proportion of cases in which infection occurs and for that reason most otologists try and guard against post-operative infection by giving systemic penicillin before and after the operation for a short while. Also, many use the sulphonamides or penicillin in the cavity afterwards. Vertigo is one of the inevitable sequelæ but this is rarely troublesome and it usually passes off slowly within three or four weeks. One other complication which must always be mentioned to a patient who is contemplating an operation is the possibility of facial palsy. The inferior lip of the fenestra is little more than one millimetre from the facial nerve in its horizontal portion and now and again some damage to the facial nerve is bound to occur. Fortunately, in the cases reported, the resulting paresis has only been temporary.

Most of the patients who are suitable for fenestration are able to hear extremely well with a hearing aid, in fact one of the main indications for operation in a case of otosclerosis is an ability to stand the fairly powerful amplification that a modern valve aid offers. Therefore, it is always advisable to make quite clear to the patient that a hearing aid will give results just as good as, if not better than, an operation.

Finally, I have no doubt that the fenestration operation, properly performed on a suitable case of otosclerosis, offers a very real chance of improvement in hearing. I think that those surgeons with the necessary experience and ability are justified in carrying out the fenestration operation, should the patient desire it, and after all the facts have been put before him.

REFERENCES

BÁRÁNY, R. (1924) *Acta otolaryng., Stockh.*, **6**, 260.
CAWTHORNE, T. (1941) *Proc. R. Soc. Med.*, **34**, 582.
FLODERUS, B. (1899) *Nord. med. Ark.*, **10**, No. 13.
GUILD, S. R. (1944) *Ann. Otol. Rhin. Laryng.*, **53**, 246.
HALL, I. S. (1944) *Proc. R. Soc. Med.*, **37**, 737.
HOLMGREN, G. (1938) "Surgical Therapy for Otosclerosis", Nelson's Loose Leaf Surgery of the Ear, New York.
HOWARTH, W. (1937) *St. Thom. Hosp. Rep.*, **2**, 153.
HUTCHINSON, C. A. (1936) *J. Laryng.*, **51**, 465.
JACK, F. L. (1894) *Trans. Amer. otol. Soc.*, **6**, 102.
JENKINS, G. J. (1913) *Int. Congr. Med.*, **17**, Sect. 16 (Otol.) Pt. 2, 609.
KESSEL, J. (1876) *Arch. Ohrenheilk.*, **11**, 199.
KISCH, H. (1912) *Proc. R. Soc. Med.*, **6**, Sect. Otol., 36.
LEMPERT, J. (1938) *Arch. Otolaryng., Chicago*, **28**, 42.
—— (1941) *Arch. Otolaryng., Chicago*, **34**, 880.
—— (1945) *Arch. Otolaryng., Chicago*, **41**, 1.
NAGER, F. R. (1928) *J. Laryng.*, **43**, 15.
PASSE, E. R. G. (1939) *J. Laryng.*, **54**, 566.
PASSOW (1897) *Verh. dtsch. otol. Ges.*, **6**, 143.
SHAMBAUGH, G. E. (1942) *J. Amer. med. Ass.*, **119**, 243.
——, and JUERS, A. L. (1946) *Arch. Otolaryng., Chicago*, **43**, 549.
SOURDILLE, M. (1932) *Rev. Laryng., Paris*, **53**, Suppl.
TOYNBEE, J. (1841) *Med.-chir. Trans.*, **24**, 190.
—— (1857) Descriptive Catalogue of Diseases of Ear, London.
WILSON, W. Personal communication.

JOINT DISCUSSION No. 1

Section of Medicine with Section of Physical Medicine

Chairman—Maurice Davidson, M.D.

(President of the Section of Medicine)

[*January* 28, 1947]

THE ÆTIOLOGY OF CHRONIC RHEUMATISM

Dr. W. S. C. Copeman: *History.*—The word arthritis is of great antiquity; it was used by Galen and his successors as indicating any affection of the joints of the body, as opposed to those of the feet for which the term podagra was used. "De Arthritide" was the title of books by Guillaume de Baillou (1591), Sennert (1631) and Schneider (1664). Arthritis being a generic term naturally included gout, which was not finally differentiated from other forms of arthritis until Sydenham did so in 1676 although de Baillou had suggested previously the possibility of the existence of other causes of chronic joint pathology. Medical thought was dominated until the seventeenth century by the humoral theory of pathology and ætiology, consequently arthritis and rheumatism were explained in terms of this hypothesis until well on into the eighteenth century, and indeed its influence is even now not entirely defunct. To Galen and his successors for many centuries rheumatism (ῥευματισμός) meant an internal discharge of a thin catarrhal humour from the blood into the joint cavities (arthritis) or elsewhere. Thus in the spring and autumn catarrhs of the respiratory mucous membranes are common and are accompanied by an external discharge of mucus, whilst a similar seasonal variation is recognized in rheumatic and gouty attacks. As is well known the word gout derived from this conception of the peccant humour being distilled drop by drop (*gutta*—drop) into the affected joints. Frederick Hoffmann (1660-1742) changed this conception somewhat by stating that "rheumatic" pain of all sorts is but a manifestation of a humour which distends the smallest blood-vessels of the affected part, so causing pain. Later writers such as Cullen (1710-90) attribute the onset of rheumatism and arthritis to the effect of cold and damp generally on a debilitated body. Later the mechanical school of Sauvages (1706-63) tended to regard arthritis as being a secondary effect of atony and rigidity of the soft tissues—fibrous tissues and muscles—surrounding and moving the affected joints. Nothing more constructive emerged until Landré-Beauvais separated the syndrome now known as *rheumatoid arthritis* from gout in 1800 under the name "goutte asthénique primitive"—no doubt out of respect for the traditional superiority of gout in this field, since he expressed his belief that they had no real connexion. *Osteo-arthritis* was first described and recognized as being a disease distinct from gout by William Heberden in his "Commentaries on Disease" published in 1802, the year after his death. It was only finally differentiated from rheumatoid arthritis in 1907 (A. E. Garrod). *Non-articular rheumatism* under the name of "chronic rheumatism" was distinguished from rheumatic fever and gout by J. Haygarth in a paper on the "Discrimination of Chronic Rheumatism from Gout, Acute Rheumatism, Scrophula, Nodosity and other Painful Diseases of the Joints and Muscles" (1813).

Ætiology of rheumatoid arthritis.—The humoral view has already been indicated, and held the field in arthritis of all types until Haygarth in a paper read to some friends in Warrington in 1779 described that "disease of joints almost peculiar to woman, and generally beginning about the period when the menses naturally cease".

Chemotherapy was a valuable adjunct or safeguard in the treatment of fenestration cases, but being in charge of a teaching clinic Dr. Hall was averse to the use of penicillin and other drugs as a routine. It seemed to him to be a reversion to the days of the carbolic spray when antiseptics rather than asepsis were the means of ensuring safety for the patient, and he preferred to rely upon a careful operative aseptic technique for his routine cases and to keep chemotherapy in reserve against the time when unusual circumstances or possibly breakdown in the technique rendered it necessary. To show learners in otology that surgical technique could not be relied upon appeared to him to be retrograde.

In only one case had Dr. Hall found that loud sounds had produced giddiness, this had been in the case of a young man who worked in a shipyard as a boiler riveter, and he found that work inside the boilers had a most unpleasant effect on him, although he was quite comfortable in an outside job.

With regard to facial palsy, Dr. Hall believed that one cause of this was working close to the facial nerve, particularly with drills of the polishing type. These drills, by the production of heat, were apt to cause temporary damage to the facial nerve, and it seemed to him that in continuous irrigation there was a safety device which would enable work to be carried on close to the nerve without any fear of damage.

In conclusion Dr. Hall wished to congratulate Mr. Passe on his film, for, having some experience of photography in the fenestration operation, he was able to appreciate the skill and care which had gone to the making of the film.

Mr. J. P. Monkhouse said that he was interested in the subject of bone conduction. He had seen a case only the other day which was not more than 10 decibels down on any frequency by air conduction, and yet there was no hearing at all by bone conduction except for two middle frequencies.

Mr. C. Hamblen-Thomas asked whether Lempert had made any examinations with the microscope of the fenestra and its surroundings in cases which had failed. It would be very interesting to know from such an examination what had been the underlying trouble. Speculation was very often wrong. He had some difficulty in getting hold of the magnifying eyeglasses, but he had discovered that they were now made in this country.

The President, in closing the discussion, said that he himself had not yet attempted this operation. Sourdille in his early work had described one in two stages and it would now be interesting to hear if this gave better results when applied to the later method of advancing the opening into the vestibule.

With regard to the use of a burr, technical information could be obtained from dental colleagues. He had been informed by one that the diamond paste burr was remarkably easy to control, a small one was efficient at slow speeds and if soft tissues were accidentally encountered they were not picked up or entwined by it.

What eventually happened to the fenestra might have to be decided in the post-mortem room. Shambaugh[1] had already reported from the laboratory what changes took place in this fistula in the monkey and he suggests that, at the present time, post-operative labyrinthitis is a more important cause of failure in the fenestration operation than bone closure.

Mr. Cawthorne had raised the question of the practical use of the hearing aid. This instrument was not popular with the deafened but its choice was a serious one if the happy results after some of these operations were not more lasting.

Mr. Cawthorne (in reply) said that first of all he would like to thank his friend and colleague—Mr. Negus—very much indeed for what he had said. He (Mr. Cawthorne) had always been very conscious of his good fortune in being associated with King's College Hospital and would always be grateful to his teachers, who included Mr. Negus, for all they had done for him.

In reply to Dr. Simson Hall he felt, with regard to the microscope, that this was a matter of choice and each surgeon would no doubt have his own preference. He (Mr. Cawthorne) had found that it was not practicable to work at a greater magnification than ten diameters and he agreed with Dr. Simson Hall that an adequate working distance was essential. With regard to chemotherapy, he felt that, as this was an open operation, prophylactic chemotherapy was justifiable and advisable. He never used prophylactic chemotherapy in closed aseptic operations such as that which he employed for Ménière's disease.

He had used a diamond paste burr for the past eight years in operations on the labyrinth and he preferred it to any other because of its gentle bite and the absence of any tendency to slip.

---

[1] SHAMBAUGH, G. E. (Jr.) (1946) *Ann. Otol. Rhin. Laryng.*, 55, 705.

JOINT DISCUSSION No. 1

Section of Medicine with Section of Physical Medicine

Chairman—MAURICE DAVIDSON, M.D.

(President of the Section of Medicine)

[*January* 28, 1947]

THE ÆTIOLOGY OF CHRONIC RHEUMATISM

Dr. W. S. C. Copeman: *History.*—The word arthritis is of great antiquity; it was used by Galen and his successors as indicating any affection of the joints of the body, as opposed to those of the feet for which the term podagra was used. "De Arthritide" was the title of books by Guillaume de Baillou (1591), Sennert (1631) and Schneider (1664). Arthritis being a generic term naturally included gout, which was not finally differentiated from other forms of arthritis until Sydenham did so in 1676 although de Baillou had suggested previously the possibility of the existence of other causes of chronic joint pathology. Medical thought was dominated until the seventeenth century by the humoral theory of pathology and ætiology, consequently arthritis and rheumatism were explained in terms of this hypothesis until well on into the eighteenth century, and indeed its influence is even now not entirely defunct. To Galen and his successors for many centuries rheumatism (ῥευματισμός) meant an internal discharge of a thin catarrhal humour from the blood into the joint cavities (arthritis) or elsewhere. Thus in the spring and autumn catarrhs of the respiratory mucous membranes are common and are accompanied by an external discharge of mucus, whilst a similar seasonal variation is recognized in rheumatic and gouty attacks. As is well known the word gout derived from this conception of the peccant humour being distilled drop by drop (*gutta*—drop) into the affected joints. Frederick Hoffmann (1660-1742) changed this conception somewhat by stating that "rheumatic" pain of all sorts is but a manifestation of a humour which distends the smallest blood-vessels of the affected part, so causing pain. Later writers such as Cullen (1710-90) attribute the onset of rheumatism and arthritis to the effect of cold and damp generally on a debilitated body. Later the mechanical school of Sauvages (1706-63) tended to regard arthritis as being a secondary effect of atony and rigidity of the soft tissues—fibrous tissues and muscles—surrounding and moving the affected joints. Nothing more constructive emerged until Landré-Beauvais separated the syndrome now known as *rheumatoid arthritis* from gout in 1800 under the name "goutte asthénique primitive"—no doubt out of respect for the traditional superiority of gout in this field, since he expressed his belief that they had no real connexion. *Osteo-arthritis* was first described and recognized as being a disease distinct from gout by William Heberden in his "Commentaries on Disease" published in 1802, the year after his death. It was only finally differentiated from rheumatoid arthritis in 1907 (A. E. Garrod). *Non-articular rheumatism* under the name of "chronic rheumatism" was distinguished from rheumatic fever and gout by J. Haygarth in a paper on the "Discrimination of Chronic Rheumatism from Gout, Acute Rheumatism, Scrophula, Nodosity and other Painful Diseases of the Joints and Muscles" (1813).

Ætiology of rheumatoid arthritis.—The humoral view has already been indicated, and held the field in arthritis of all types until Haygarth in a paper read to some friends in Warrington in 1779 described that "disease of joints almost peculiar to woman, and generally beginning about the period when the menses naturally cease".

In 1805 he expanded this in a published tract calling it "nodosity of the joints" and quoting 34 cases all but one in women. This would seem to foreshadow the role subsequently assigned by some later observers to the endocrine system in rheumatoid arthritis. Fuller in his book on "Rheumatism, Rheumatic Gout and Sciatica" (1852) agreed that the real factor must be a general blood poison, to the formation of which cold, debility and other conditions might conduce. The chemical view in the middle of the nineteenth century which postulated an excess of uric acid in the blood and tissues (or lactic acid—Todd), was introduced by Haigh, and enjoyed brief popularity. The name rheumatoid arthritis was coined in 1859 by Sir A. B. Garrod, and it is perhaps of interest to quote his reasons for doing so. He states that the term rheumatic gout is given to a disease having a peculiar pathology in no way related to gout, and not necessarily to rheumatism—and which is sometimes termed chronic rheumatic arthritis. He then says ". . . although unwilling to add to the number of names, I cannot help expressing a desire that one might be found for this disease . . . perhaps *Rheumatoid Arthritis* would answer the object, by which term I should wish to imply an inflammatory affection of the joints not unlike rheumatism . . . but differing materially from it". He considered its causation to be "exposure to the influence of powerful depressing causes, either mental or physical, and sometimes possibly by subacute rheumatic fever". He showed that there is no excess of uric acid present in the blood.

During the last third of the century, before the rise of bacteriology, the influence of the C.N.S. was invoked by Charcot (1868) and later by Pierre-Marie largely as the result of its bilateral and symmetrical distribution and its selective action on the small muscles of the hands. He also first drew attention to its centripetal mode of progression. The neurotrophic hypothesis associated with the name of Weir Mitchell also lingered on until the end of the century as evidenced by J. K. Spender's opinion in 1897 that "Rheumatoid Arthropathy" would have been a better name for rheumatoid arthritis had Garrod only adopted it instead of the latter in 1859. He regarded the disease as a neurosis. The current view at this time as expressed in Allbutt's great "System of Medicine" (1896 edition) was that rheumatoid arthritis was primary or secondary. Primary types resulted from general weakness due to mental wear and tear and worry, too frequent child-bearing, unfavourable hygiene, &c., and it often appeared as a sequel of influenza (of which outbreaks were common at that time). It is stated that "the term primary rheumatoid arthritis is justified by the fact that a state of the system and of the general health has been brought about which is favourable to a degenerative process . . . in addition there is the grave poisoning of nerve centres, and the disturbed nutrition which is the result". The interesting observation is made that "rheumatoid disease is a near neighbour of tuberculosis; and when a proclivity to tuberculosis exists in a family we may expect that any rheumatic member of that family may become rheumatoid". Secondary rheumatoid arthritis is stated to be "a special form which occurs after rheumatic fever—a sequence which justifies the adjective rheumatoid".

In 1909 A. E. Garrod introduced the metabolic factor as being causative of certain forms of chronic arthritis other than gout, a hypothesis which was taken further by Pemberton in 1912 who found metabolic disturbances in the form of lowered sugar tolerance in 60% of his cases of rheumatoid arthritis.

The infective hypothesis was initiated by Benjamin Rush, an American physician, who in 1803 cured a case of rheumatoid arthritis (?) of the hip by the removal of an aching tooth. In 1896 Bannatyne, Wohlmann and Blaxall described 100 cases of rheumatoid arthritis from which they had isolated a small bacillus with polar staining which they believed to be causative. In 1904 Goldthwait of Boston split off infective arthritis in his classification as being distinct from rheumatoid arthritis, of which the cause was said to be "idiopathic".

Soon after Still's description of the juvenile form of rheumatoid arthritis in 1896, Bannatyne *et al.* stated their belief—which was that also of Still himself—that the glandular enlargement seen in this form of disease is important evidence of infection.

Infective arthritis.—The rise of bacteriology in the last quarter of the nineteenth century led to the recognition of a large group of specific infective arthritides including gonococcal, streptococcal and dysenteric. Tuberculous arthritis had been recognized and described before this period on clinical grounds notably by Richard Wiseman, surgeon-in-ordinary to King Charles II, who thought it could be cured by the royal touch in common with the more banal manifestations of scrofula. It will be remembered also that Percival Pott wrote on tuberculosis of the spine in 1779, giving rise to the name Pott's disease. In this connexion may be mentioned also the belief of Poncet (1849-1913) that a tuberculous focus in the body will, under certain circumstances, give rise to a polyarthritis which is indistinguishable from rheumatoid arthritis of other causation, and sometimes other forms of joint disease including hypertrophic pulmonary osteo-arthropathy.

References to the role of syphilis in causing arthritis manifestations are to be found very soon after its establishment in Europe. Villalobos (1473-1560) and Fallopius (1523-62) are quoted by Rolleston. J. Russell of Edinburgh referred in 1802 to syphilitic arthritis, whilst Clutton's famous description of arthritis of the knee-joints in 1886 showed that congenital syphilis could also be held responsible for certain types of arthritic manifestations.

William Hunter (1861-1937) was the first observer to point out the possible remote effects, including arthritis, of focal—especially oral—sepsis. This hypothesis was much popularized by the late Sir William Willcox but has been used perhaps to explain too much.

ÆTIOLOGY OF OSTEO-ARTHRITIS

Although osteo-arthritis is a very ancient disease it was not clinically differentiated from other forms of arthritis until Cruveilhier did so in his paper published in 1829 entitled "Usure des Cartilages articulaires". He attributed the cause to inflammation, an opinion which was shared by most subsequent writers including Adams (1857), until Goldthwait (1904) stated his view that it is a constitutional affection with local joint manifestations which may be polyarticular—a view which would nowadays perhaps be considered to be more applicable to rheumatoid arthritis. Stockman in 1920 summarized the current view in the words "The cause of chronic osteo-arthritis is not known. Its onset has been attributed to cold and damp, trauma, previous joint disease, heredity and senile changes, but these can at most only be regarded as causes predisposing to the very definite and specific alterations which take place in the joints". I doubt if my colleagues will be able to advance very much upon this dictum of twenty-seven years ago!

In 1933 Lawford Knaggs working on Strangeway's specimens in the Royal College of Surgeons concluded that rheumatoid and osteo-arthritis merge clinically and pathologically and are expressions—at opposite ends of the same scale—of a single disease, which is toxic in origin.

Non-articular rheumatism.—Balfour writing in 1816 quotes Cullen's (1710-90) views on the ætiology of chronic rheumatism, in which category no doubt the non-articular forms are included. Cullen gives it as his opinion that it originates from a morbid affection producing congestion of the capillaries, tending to "an atony both of the blood-vessels and of the muscular fibres of the part affected, together with a degree of rigidity and contraction in the latter, such as frequently attends them in a state of atony". Balfour says: "Thus exposure to cold produces in one person catarrh, in another pneumonia, in another pleuritis, in another rheumatism, according to idiosyncrasy . . . moreover chronic is also often the consequence of acute rheumatism."

Little or no variation on this theme is found in other literature until we come to Stockman's view (1920) that fibrositis is the result of preceding general infections, or of local inflammations or injuries.

BIBLIOGRAPHY

ADAMS, R. (1857) A Treatise on Rheumatic Gout. London.
ALLBUTT, T. CLIFFORD. A System of Medicine. London (1896 edition).
BANNATYNE *et al.* (1896) *Lancet* (i), 1120.
BAILLOU, G. de (1642) Opera Omnia. Liber de Rheumatisme.
CHARCOT, J. M. (1868) *Arch. Physiol.*, **1**, Paris.
CLUTTON, H. (1886) *Lancet* (i), 516.
CRUVEILHIER, J. (1829) Anatomie Pathologique. Liv. ix, pl. 6.
FULLER, T. (1852) On Rheumatism, Rheumatic Gout and Sciatica. London.
GARROD, A. B. (1859) Gout. London.
GARROD, A. E. (1907) Allbutt's System of Medicine. London.
—— (1909) Inborn Errors of Metabolism. London.
GOLDTHWAIT, J. E. (1904) *Boston med. surg. J.*, **151**, 529.
—— PAINTER, J., and OSGOOD, R. (1910) Diseases of the Bones and Joints. Boston.
HAYGARTH, J. (1805) A Clinical History of Nodosity of the Joints. London.
HEBERDEN, W. (1802) Commentaries on the History and Cure of Disease. London.
HOFFMANN, F. (1748) Opera Omnia II.
HUNTER, W. (1901) Oral Sepsis. London.
KNAGGS, L. (1933) *Brit. J. Surg.*, 20, 309.
LANDRÉ-BEAUVAIS, A. J. (1800) Doit-on admettre une nouvelle espèce de goutte sous la dénomination de goutte asthénique primitive ? Paris (Thesis).
PEMBERTON, R. (1912) *Amer. J. med. Sci.*, **144**, 474.
PONCET, A. (1900) *Lyon méd.*, 93, 228.
RUSH, B. (1809) Medical Enquiries and Observations. Philadelphia.
RUSSELL, J. (1802) A Treatise on the Morbid Affections of the Knee Joint. Edinburgh.
SANDAMORE, C. (1827) Treatise on Rheumatism. London
SPENDER, J. K. (1897) Article in Allbutt's System of Medicine. London.
STOCKMAN, R. (1920) Rheumatism and Arthritis. Edinburgh.
SYDENHAM, T. (1848) Medical Observations (R. Latham's translation) Sydenham Society Library.

Dr. Philip Ellman: Our first step before we discuss the ætiology of chronic rheumatism is to attempt a definition and simple classification of chronic rheumatism although precision, in our present state of knowledge, is not possible. I cannot, unfortunately, include to-day a discussion of rheumatic fever, although I am personally of the opinion that the evidence continues to reinforce the unitary theory originally propounded by Jonathan Hutchinson and Poynton that the rheumatisms in the restricted sense in which we shall employ the term are allied to one another and constitute a family group among diseases due to some common weakness. Chronic rheumatism comprehends a group of diseases of the locomotor system characterized by pain and stiffness and, where joints are involved, by local swelling. General constitutional disturbance may or may not be present, depending on the nature of the lesion, and the onset, while usually insidious, may also be acute. The ensuing diseases of chronicity become, when untreated, associated with crippledom of varying degree. In view of their unknown ætiology a better designation is probably non-specific diseases of the joints and related structures.

Endless classifications—in the neighbourhood of sixty—have been introduced by numerous committees and have produced much confusion. My own preference is for a return, with slight modifications, to the classification originally propounded by Sir Archibald Garrod in 1890. He recognized two essential types of chronic non-specific arthritis, viz. rheumatoid arthritis and osteo-arthritis, more correctly described as degenerative arthrosis. If we include also non-articular rheumatism and bear in mind the less common chronic specific arthritides we have the basis upon which are built the simpler English and American classifications. The more specialized classification devised by a committee of the Royal College of Physicians in 1934 is the most comprehensive and scientific to date.

Analogy with tuberculosis.—The so-called chronic rheumatic diseases present a problem comparable in magnitude and significance to tuberculosis, with which they have much in common: they are responsible for much social and economic disturbance with infinite misery, disability and invalidism, more often than not occurring in the prime of life of the breadwinner of the family. But, while tuberculosis is an infectious disease of known ætiology associated with mortality, chronic rheumatism is, on the other hand, a disease of unknown ætiology associated with morbidity. It has hitherto been relegated to the list of uninteresting and incurable diseases and has been treated in the main almost with indifference by the profession, although few would contest that a life of helplessness, total incapacity with the patient a burden to himself, his family and society, is worse than death.

Nevertheless, the prevailing general attitude of defeatism in relation to the rheumatic diseases in general and to chronic arthritis in particular is quite unjustified. At present in-patient and out-patient facilities and provision for teaching and research are hopelessly inadequate. It is my firm conviction—and I may be pardoned for being somewhat provocative—that the rheumatic diseases are primarily the concern of the general physician, working closely with the general practitioner, rather than of the ultra-specialist, and they must resume their rightful place within the province of general medicine if they are to be successfully controlled. Only in this way will the patient be viewed as a whole, for these diseases are, like tuberculosis, systemic diseases producing local manifestations in the joints instead of the lungs, and both simulating, at one time or another, almost any other disease in general medicine.

Regarding the exact ætiology of chronic rheumatism we are regrettably in precisely the same position now as we were with tuberculosis in 1882 before Koch had discovered the tubercle bacillus. Many factors have been incriminated as ætiological and a vast amount of literature of a critical and non-critical nature continues to arise. While I propose to deal more particularly with environmental factors (occupational, physical and mental), for I believe with Ryle (1947) that the development of ætiological science must now be based more and more upon sociomedical investigation, I would like, however, to deal first with a few prevailing concepts.

First, *focal infection* with special reference to the rheumatoid type of arthritis: Of the last 100 cases attending the Rheumatism Unit at St. Stephen's Hospital, London County Council, the duration of whose disease varied from six months to twenty-five years and averaged 6·1 years, many were found to be divested of teeth and tonsils, some with sinuses drained, gall-bladder, appendix, and other organs removed. Yet in spite of such radical measures in dealing with supposed focal infection the patient was frequently no better but, on the contrary, despondent and lowered in morale. I calculated that no more than 3% of these 100 cases had genuinely benefited from such treatment, but in such cases of so-called secondary focal infective arthritis removal of a carefully assessed focus of sepsis may produce a dramatic response. Similar enthusiasm has even been extended to the osteoarthritic type of disease where, it would be generally agreed, focal infection can play no appreciable part. Non-articular rheumatism has likewise suffered similar insults in varying degree. There is surely need for a complete revaluation of the focal infection theory. I would urge the need for a more conservative and discriminating attitude in the final analysis. The work of Vaizey and Clark Kennedy, among many others, has supplied an admirable corrective in relation to chronic rheumatism and, having disposed of many of the prevailing ideas, they point out that the cure of according to idiosyncrasy . . . moreover chronic is also often the consequence of acute rheumatism."

Little or no variation on this theme is found in other literature until we come to Stockman's view (1920) that fibrositis is the result of preceding general infections, or of local inflammations or injuries.

BIBLIOGRAPHY

ADAMS, R. (1857) A Treatise on Rheumatic Gout. London.
ALLBUTT, T. CLIFFORD. A System of Medicine. London (1896 edition).
BANNATYNE *et al.* (1896) *Lancet* (i), 1120.
BAILLOU, G. de (1642) Opera Omnia. Liber de Rheumatisme.
CHARCOT, J. M. (1868) *Arch. Physiol.*, **1**, Paris.
CLUTTON, H. (1886) *Lancet* (i), 516.
CRUVEILHIER, J. (1829) Anatomie Pathologique. Liv. ix, pl. 6.
FULLER, T. (1852) On Rheumatism, Rheumatic Gout and Sciatica. London.
GARROD, A. B. (1859) Gout. London.
GARROD, A. E. (1907) Allbutt's System of Medicine. London.
—— (1909) Inborn Errors of Metabolism. London.
GOLDTHWAIT, J. E. (1904) *Boston med. surg. J.*, **151**, 529.
—— PAINTER, J., and OSGOOD, R. (1910) Diseases of the Bones and Joints. Boston.
HAYGARTH, J. (1805) A Clinical History of Nodosity of the Joints. London.
HEBERDEN, W. (1802) Commentaries on the History and Cure of Disease. London.
HOFFMANN, F. (1748) Opera Omnia II.
HUNTER, W. (1901) Oral Sepsis. London.
KNAGGS, L. (1933) *Brit. J. Surg.*, 20, 309.
LANDRÉ-BEAUVAIS, A. J. (1800) Doit-on admettre une nouvelle espèce de goutte sous la dénomination de goutte asthénique primitive ? Paris (Thesis).
PEMBERTON, R. (1912) *Amer. J. med. Sci.*, **144**, 474.
PONCET, A. (1900) *Lyon méd.*, **93**, 228.
RUSH, B. (1809) Medical Enquiries and Observations. Philadelphia.
RUSSELL, J. (1802) A Treatise on the Morbid Affections of the Knee Joint. Edinburgh.
SANDAMORE, C. (1827) Treatise on Rheumatism. London
SPENDER, J. K. (1897) Article in Allbutt's System of Medicine. London.
STOCKMAN, R. (1920) Rheumatism and Arthritis. Edinburgh.
SYDENHAM, T. (1848) Medical Observations (R. Latham's translation) Sydenham Society Library.

Dr. Philip Ellman: Our first step before we discuss the ætiology of chronic rheumatism is to attempt a definition and simple classification of chronic rheumatism although precision, in our present state of knowledge, is not possible. I cannot, unfortunately, include to-day a discussion of rheumatic fever, although I am personally of the opinion that the evidence continues to reinforce the unitary theory originally propounded by Jonathan Hutchinson and Poynton that the rheumatisms in the restricted sense in which we shall employ the term are allied to one another and constitute a family group among diseases due to some common weakness. Chronic rheumatism comprehends a group of diseases of the locomotor system characterized by pain and stiffness and, where joints are involved, by local swelling. General constitutional disturbance may or may not be present, depending on the nature of the lesion, and the onset, while usually insidious, may also be acute. The ensuing diseases of chronicity become, when untreated, associated with crippledom of varying degree. In view of their unknown ætiology a better designation is probably non-specific diseases of the joints and related structures.

Endless classifications—in the neighbourhood of sixty—have been introduced by numerous committees and have produced much confusion. My own preference is for a return, with slight modifications, to the classification originally propounded by Sir Archibald Garrod in 1890. He recognized two essential types of chronic non-specific arthritis, viz. rheumatoid arthritis and osteo-arthritis, more correctly described as degenerative arthrosis. If we include also non-articular rheumatism and bear in mind the less common chronic specific arthritides we have the basis upon which are built the simpler English and American classifications. The more response to the same noxious agent may be manifested. Recently I have had in hospital several cases of rheumatoid arthritis complicated by rheumatic carditis with mitral stenosis. Taking 100 consecutive cases of the rheumatoid type of arthritis in my series I find that 8 of them had co-existent rheumatic carditis and I have notes of 22 further cases where rheumatic carditis (mainly with mitral stenotic lesions) has co-existed. This is in striking contrast to the extremely high incidence of rheumatic heart disease discovered by the autopsy studies of Young and Schwedel (1944), Bagenstross and Rosenberg (1941) and Bayles (1943) where the respective incidences were 65%, 56% and 22%. In Still's original cases of juvenile rheumatoid arthritis he reported several cases of pericardial adhesions. I have encountered at least one patient gravely ill with an acute fibrinous pericarditis who recovered, and Granirer (1946) reports a case of pericardial effusion with rheumatoid arthritis in which there was no history of rheumatic fever.

These and other studies suggest that in a large number of cases of slow progressive joint involvement cardiac lesions may be clinically silent, thereby escaping recognition. It has for some years been my practice to make a routine examination of the cardiovascular system in every case of rheumatoid arthritis and although my figures are only 8% (for clinical examination alone) I believe they are not insignificant in the light of existing literature. Should autopsy studies become more readily available, they may assist in establishing, as Young and Schwedel have already postulated, a "rheumatic state", probably highly dependent on age, with varying degrees of vulnerability of the heart and joints. I feel that the recently established Royal College of Physicians' Committee on acute rheumatism might well have had its terms of reference extended to include an investigation of its possible connexion with chronic rheumatism.

Systemic factors in rheumatoid arthritis.—In the rheumatoid type of arthritis, the systemic aspect of the disease is often of paramount importance. For example, in Felty's syndrome the accompanying lymphadenopathy, the leukopenia, splenomegaly, and sometimes hepatomegaly are interesting visceral accompaniments of the rheumatoid type of arthritis. The question arises whether these are manifestations of hypersensitivity. In this connexion I should like to refer to a case recently under my care, which I hope to publish in detail later, which proved to be one of Felty's syndrome. The case was characterized by a rheumatoid type of arthritis, splenomegaly, and hepatomegaly, lymphadenopathy and, later, a widespread purpura; at no time was there a leukopenia. The condition was complicated by a diffuse chronic pulmonary lesion, the radiological appearances of which were variously interpreted as compatible with Boeck's sarcoidosis, or with a pneumokoniosis (there was no history of an occupational hazard). Dr. Peter Kerley, who kindly saw the films with me, regarded the appearances as compatible with a periarteritis, an interesting suggestion in the light of a possible connexion between periarteritis and rheumatoid arthritis to which I will refer later. Autopsy findings confirmed the Felty's syndrome and, as far as the lungs were concerned, gave no evidence of sarcoidosis. They showed evidence of a curious chronic fibrosing bronchopneumonic lesion. Can this be interpreted as tissue hypersensitivity in the lung in keeping with hypersensitivity manifested elsewhere in the body? Dr. Robb-Smith, who kindly saw the sections for me, raised this as a possibility. I know of no comparable case in the literature.

In the light of such an interpretation of Felty's syndrome one is led to speculate on what is the essential difference, if any, in the pathogenesis of such conditions closely allied to rheumatoid arthritis as spondylitis ankylopoietica, psoriasis arthropathica, and Reiter's syndrome of non-specific arthritis, urethritis and conjunctivitis. The work of Rich and his co-workers has indicated an even wider association, on the basis of hypersensitivity between the rheumatoid type of arthritis and such rheumatoid arthritis following dental extraction is the exception rather than the rule and that bad teeth are not incompatible with good general health.

Time will not permit me to refer in detail to the extensive recent literature on ætiology in relation to *virus infection* and the theory of bacterial allergy with the interesting experimental work of Angevine, Rothbard and Cecil, Rich and his co-workers which merits attention. Schlesinger and his colleagues in 1935 mooted the possibility of a virus as the cause of rheumatic fever, a conception upheld by Eagles, Timbrell Fisher and others and extended also to rheumatoid arthritis. Sabin at the Rockefeller Institute has further confirmed this experimental work.

Basically, in the *bacterial allergy theory*, the acute and chronic rheumatisms are regarded as anaphylactic diseases with multiple lesions in the mesodermal system produced by continual antigen-antibody reactions in or on tissue cells. Visceral and other lesions may be explained as hypersensitivity manifestations in tissues elsewhere in the body. Levinthal believes that the debility of the antibody-producing system—the reticulo-endothelial system—is the basic cause of rheumatism and that all other indirect or precipitating factors interfere with the function of antibody production and with the capacity of reacting or maintaining the state of perfect immunity. The concept is attractive, appears rational and lends support to the unitary theory. It offers some co-ordination for the rheumatic group of diseases and suggests a relationship between the acute rheumatoid type of arthritis and rheumatic fever. It is possible, too, that the syndromes of a recurrent and transitory nature included under the term "palindromic rheumatism" of Hench and Rosenberg (1944) can be widened still further to include the so-called intermittent hydro-arthrosis, serum joint disease, allergic arthritis and allied syndromes as suggested by Parkes Weber, 1946. With regard to the so-called allergic arthritis it is not without interest to recall two long-standing cases of asthma who subsequently developed a typical rheumatoid type of arthritis with no recurrence of their asthma.

The following two cases of allergic arthritis and intermittent hydro-arthrosis which have recently come under my care are of interest in this connexion:

F. C. E., male, age 53. *Physical history.*—Perfectly healthy all his life until nine weeks ago when he received an injection of anti-catarrhal vaccine. Four days later there was an acute onset of knife-like pain in the left knee-joint, which became red, swollen, and tender, necessitating complete rest in bed for one week. During the next week he had acute and severe pains in the left ankle and both hips. These cleared with rest in a further fortnight. When he was seen, six weeks after the onset, the left knee-joint was still swollen and a large effusion was present. He had had 4 injections of the vaccine at weekly intervals and two days after each he had developed an urticarial rash. There was nothing noteworthy in the family or previous history. The blood uric acid was 5·6 mg. Uric acid in the joint fluid was 5·77 mg.%.

The presumptive diagnosis is that of gouty arthritis precipitated by an allergic response to foreign protein.

H. A. H., male, aged 41.—Thirteen years ago, following a minor injury, he had swelling of the left knee-joint which cleared spontaneously. Five years ago he fell on the right knee following which there was an effusion which did not clear for three months in spite of strict rest. Three years ago a recurrent swelling of the right knee followed a route march while on Home Guard exercises. Since that time there has been a persistent effusion of the right knee-joint of varying extent, increased by exercise and reduced slightly during periods of rest. On November 26, 1946, swelling and effusion occurred spontaneously in the left knee-joint as well and one week later he had bilateral hydro-arthrosis. Fourteen days later he complained of severe malaise and felt as if he were convalescent from a serious illness. On examination, in addition to swelling and recurrent effusion of the knee-joint there was pitting œdema of the left leg and ankle. He had no hæmorrhages or purpuric spots. There was no noteworthy previous or family history.

The heart and rheumatoid arthritis.—Rich and his associates have suggested that the basic characteristics of both rheumatic carditis and arthritis result from anaphylactic hypersensitivity and I have been struck, particularly during the war years, with the number of borderline cases lying between acute rheumatism and the rheumatoid type of arthritis. The inference to be drawn is that a variable tissue lationship to the circulating blood, the chemistry and cytology of various forms of arthritis, and, more generally, the metabolic activities of tissues taking part in the construction of joints, e.g. nutrition of the articular cartilage and respiration in articular cartilage: permeability of synovial membrane and articular cartilage are further problems awaiting the research worker. Each and all of these may contribute towards the ultimate goal of determining the exact ætiology of this group of diseases.

ENVIRONMENTAL FACTORS

The chronic rheumatic diseases have a long and extensive history. The skeletal remains of prehistoric man show that these diseases were among the hazards of the earliest human life—arthritis has, in fact, been discovered among the triassic dinosaurs. Studies of arthritis in wild animals show that rheumatism may develop not only when they are in captivity but also in their native habitat, occurring in both herbivorous and carnivorous animals.

Climate.—With regard to geographical distribution and climate it is generally accepted that chronic rheumatism is a disease of temperate climates and becomes diminishingly common as the equator is approached. On the other hand the interaction of dampness and rheumatism remains a controversial subject. Most probably damp has a deleterious effect on normal skin functions and may encourage catarrh and nasopharyngeal infections, thereby weakening resistance. In spite of this possibility, the general privation of trench life in Flanders from 1914-18 produced few cases of rheumatism among the troops. It is possible that damp surroundings may produce symptoms in a latent case of rheumatism, and although it is almost universally agreed that a damp house is detrimental to health it is not yet fully understood how it fosters the development of rheumatic disease. From a wide experience of the histories of rheumatic subjects I have known cases occurring in a damp house and becoming aggravated under such conditions but improving on removal to dryer surroundings. Damp, cold and other states of the atmosphere are believed to influence the development of rheumatic disease but Leonard Hill has often pointed out that dirt, artificially heated and ill-ventilated houses, overcrowding, &c., are more potent as causal factors than external weather conditions. Lack of a protective diet, as is seen in so many dietetic histories, may certainly be an accessory to the development of the disease although on the positive side there is no known specific diet.

Social history.—The art of taking a complete history is emphasized as one of fundamental importance in the course of medical teaching, but the extent to which such instruction is practised in later life is a matter for conjecture. One is, in fact, led to wonder how many of us make a really detailed investigation of the daily habits and environment of our patients. We should discover the previous, the family, the social and environmental histories (including physical, mental, occupational, hygienic, and dietetic factors), all of which may be ætiologically significant. As Professor Henry Cohen stated in a recent Skinner Lecture: "Such inquiries alone can unmask the evolution of disease and significance of the present state as revealed by examination. The eliciting of an accurate history reveals the quality of the practising physician. It demands care and courtesy, time and patience: the failure to take careful histories is in no small measure an expression of the economic structure of the present-day practice of medicine with its resultant hurry."

The interdependence of social, environmental and clinical studies and the contribution which a trained health visitor or social worker can make to a better evaluation of causal factors has for long been appreciated in the sphere of tuberculosis. Experience suggests the need for a comparable service in relation to the rheumatic diseases. Information so obtained makes it possible to assess the in-conditions as acute disseminated lupus erythematosus, periarteritis nodosa, dermatomyositis and scleroderma. Their work may ultimately lead to a better appreciation of these hitherto obscure conditions.

THE ENDOCRINAL FACTOR

The adrenals.—The experimental production by Selye and his co-workers of a polyarthritis, resembling histologically that seen in rheumatic fever and even in rheumatoid arthritis, following desoxycorticosterone acetate, demonstrates the role of the adrenal glands and has focused attention upon the endocrines. Urbach has even suggested that this may be an allergic reaction, i.e. the pathological lesions may be the clinical expression of an allergy to the adrenal cortex.

Thyroid.—As far as the thyroid is concerned the question arises whether the co-existence of hyperthyroidism in a rheumatoid subject is more than a coincidence. In the osteo-arthritic type of lesion the association of hypothyroidism is, in my experience, not uncommon. A syndrome of obesity, degenerative arthritis, and hypertension is frequently encountered in women at or about the menopause, such subjects also manifesting a raised blood cholesterol and a low basal metabolic rate. The response to thyroid medication is frequently dramatic.

The pituitary.—The part played by the pituitary and other endocrines is well seen in women. Rheumatic symptoms seem often to be exacerbated before the menses while during pregnancy there is frequently remission. I have no record of arthritis developing during pregnancy while Hench has described cases that have become pregnant as a therapeutic measure. The development of menopausal arthralgias with no joint changes is well recognized and usually responds to stilbœstrol. The rheumatoid type of arthritis may occur at this age-period although a degenerative type of joint disease, such as the syndrome already described, is more usual.

The potential significance of the pituitary in relation to chronic rheumatism has received considerable attention and has raised hopes concerning X-ray irradiation of the pituitary in the treatment of rheumatoid arthritis. Over-activity of the pituitary has been incriminated in certain cases of chronic arthritis of the osteo-arthritic type. In acromegaly an associated spondylitis is well known. In Cushing's disease joint lesions are known to occur. The relationship of acromegaly to pulmonary osteo-arthropathy has been noted by Fried in his work on lung cancer; he has made the interesting suggestion that the diffuse pulmonary osteo-arthropathy found in some cases is probably due to a dyspituitarism akin to acromegaly. In this connexion I would like to record the case of a man aged 55 referred to the Rheumatism Unit at St. Stephen's Hospital on account of pain, swelling and stiffness of both knees. Examination revealed a rheumatoid type of lesion with effusions into both knee-joints. The condition was complicated by a gross pulmonary osteo-arthropathy with an ossifying periostitis of the radius, ulna, femora, tibiæ and fibulæ. The patient also had a clubbed nose. Examination of the chest showed a right upper lobe bronchial carcinoma. Almost immediately following the removal of the growth by a lobectomy performed by Mr. Brock his knee-joint swellings began to subside, his fingers and nose became less clubbed, and now, after nearly two years, there is marked reduction of the subcutaneous tissue in the region of the terminal phalanages with practically normal fingers and toes. I have had two similar cases under my care.

Studies of joint anatomy, physiology, and pathology in relation to ætiology.—Such studies of the joint cavities and their related structures are frequently necessary with special reference to the synovial membrane and fluid and articular cartilage. Further investigations may include the origin of synovial fluid, its function, its re-

ONE HUNDRED CASES OF RHEUMATOID ARTHRITIS: ENVIRONMENTAL FACTORS CAUSING RELAPSES

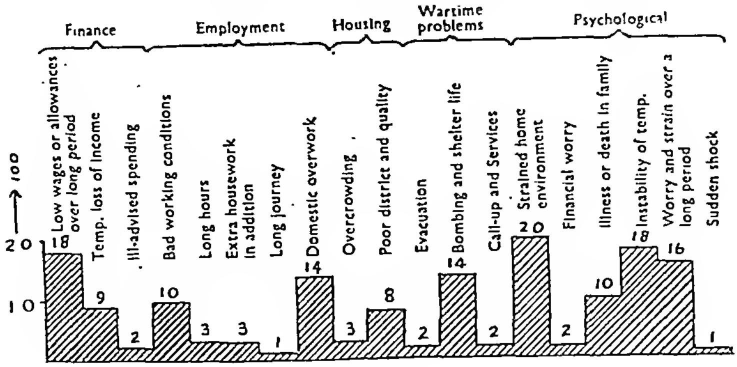


CHART III.

housewives (over 57%). Of 135 cases of rheumatoid arthritis under my care at the Leatherhead Emergency Hospital 62% (100 female cases) were housewives. Nevertheless, it is apparent that psychological problems are more outstanding than either employment or wartime problems. Physical trauma is, in my view, a major contributory ætiological factor in the osteo-arthritic type of disease and careful inquiry will often reveal such traumata in relation to occupation.

The age and sex incidence.—The following figures of 241 civilian cases admitted to the Leatherhead Emergency Hospital between September 1939 and September 1946 are of interest regarding the incidence of chronic rheumatism. The 178 female and 63 male cases can be classified as follows:

LEATHERHEAD EMERGENCY HOSPITAL

	Total no. of cases	Female	Male	Age range	Average age
Rheumatic fever	3	2	1		17
Chronic arthritis (rheumatoid type)	135	100	35	17–78 (f)	49
				15–74 (m)	45
Chronic arthritis (osteo-arthritic type) ..	65	53	12	32–89 (f)	60
				40–77 (m)	64
Non-articular rheumatism ..	34	22	12	15–81 (f)	46
				26–69 (m)	44
Gouty arthritis	4	1	3		59

ST. STEPHEN'S HOSPITAL (RHEUMATISM UNIT)

In-patients

Cases of Rheumatoid Type of Arthritis

	Total no. of cases	Age range	Average age
1945.. ..	45	21–72 (f)	47
		15–69 (m)	46
1946.. ..	50	22–65 (f)	48
		25–75 (m)	46

It will be seen that the average age range is fairly constant. The preponderance of women over men of all my in-patients and out-patients with a rheumatoid type of arthritis is roughly in the ratio of 3:1. L. S. P. Davidson in a series of 270 cases found 70% females and 30% males. Among osteo-arthritics my figures at the Leatherhead Emergency Hospital also show a preponderance of females but this may well be due to the particular circumstances prevalent during the war. My general experience does not show so high a disparity between the sexes. As far as age is concerned, generally speaking, cases of the rheumatoid type are seen fluence of social, domestic, physical, mental or industrial maladjustment in the origin and development of disease. It is not without interest to review the environmental factors obtained from social histories preceding the onset of disease in 100 cases of the rheumatoid type of arthritis between 1942 and 1944 (Chart I) and another 100 cases between 1944 and 1946 (Chart II) and also in relation to relapse of the disease in a third 100 cases (Chart III). The influence of finance, employment, housing, wartime problems, domestic, occupational, and psychogenic factors can be appreciated from these three charts. It will be noted that psychological factors are highest in both groups, that wartime problems are particularly marked on the second chart which covers the flying-bomb period when war strain was maximal. The effect of long hours is also marked in the 1944-46 group and from the occupational standpoint the incidence is seen to be extremely high among

ENVIRONMENTAL FACTORS PRECEDING ONSET OF RHEUMATOID ARTHRITIS IN 100 CASES SEEN 1942-1944 (CHART I) AND IN 100 CASES SEEN 1944-1946 (CHART II)

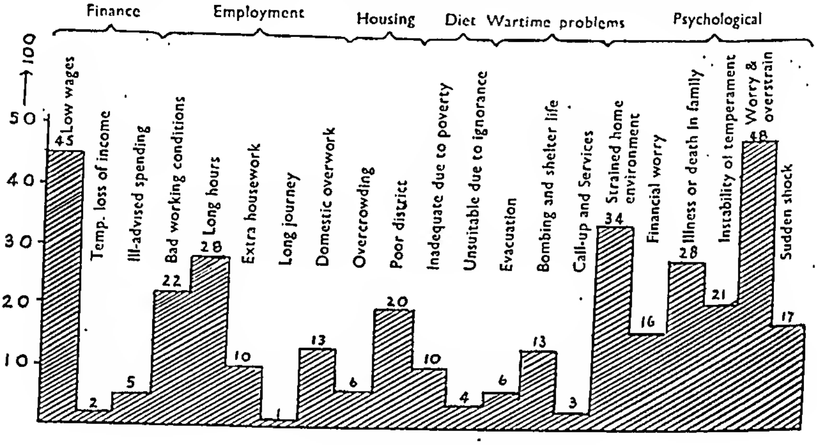


CHART I.

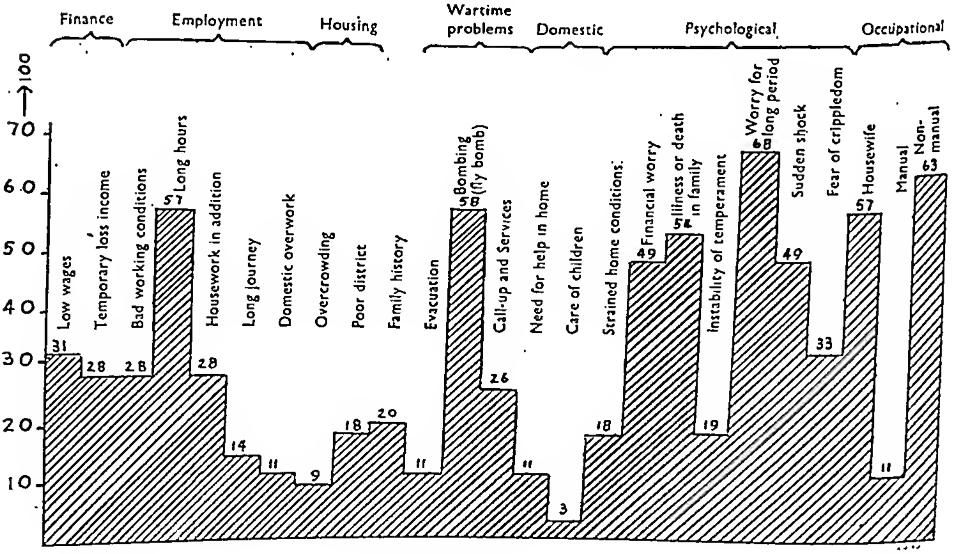


CHART II.

ONE HUNDRED CASES OF RHEUMATOID ARTHRITIS: ENVIRONMENTAL FACTORS CAUSING RELAPSES

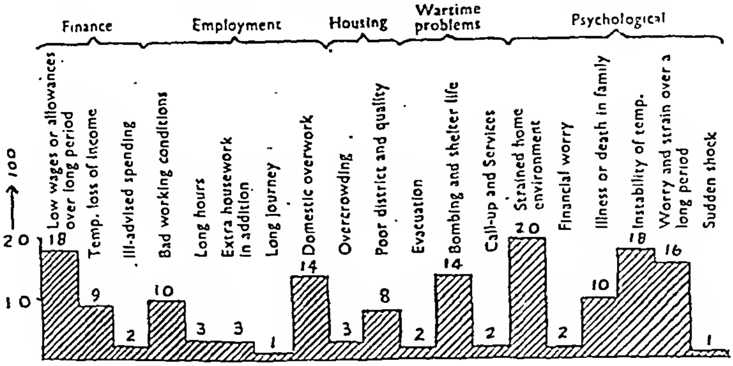


CHART III.

housewives (over 57%). Of 135 cases of rheumatoid arthritis under my care at the Leatherhead Emergency Hospital 62% (100 female cases) were housewives. Nevertheless, it is apparent that psychological problems are more outstanding than either employment or wartime problems. Physical trauma is, in my view, a major contributory ætiological factor in the osteo-arthritic type of disease and careful inquiry will often reveal such traumata in relation to occupation.

The age and sex incidence.—The following figures of 241 civilian cases admitted to the Leatherhead Emergency Hospital between September 1939 and September 1946 are of interest regarding the incidence of chronic rheumatism. The 178 female and 63 male cases can be classified as follows:

LEATHERHEAD EMERGENCY HOSPITAL

	Total no. of cases	Female	Male	Age range	Average age
Rheumatic fever	3	2	1		17
Chronic arthritis (rheumatoid type)	135	100	35	17–78 (f)	49
				15–74 (m)	45
Chronic arthritis (osteo-arthritic type)	65	53	12	32–89 (f)	60
				40–77 (m)	64
Non-articular rheumatism	34	22	12	15–81 (f)	46
				26–69 (m)	44
Gouty arthritis	4	1	3		59

ST. STEPHEN'S HOSPITAL (RHEUMATISM UNIT)

In-patients

Cases of Rheumatoid Type of Arthritis

	Total no. of cases	Age range	Average age
1945	45	21–72 (f)	47
		15–69 (m)	46
1946	50	22–65 (f)	48
		25–75 (m)	46

It will be seen that the average age range is fairly constant. The preponderance of women over men of all my in-patients and out-patients with a rheumatoid type of arthritis is roughly in the ratio of 3:1. L. S. P. Davidson in a series of 270 cases found 70% females and 30% males. Among osteo-arthritics my figures at the Leatherhead Emergency Hospital also show a preponderance of females but this may well be due to the particular circumstances prevalent during the war. My general experience does not show so high a disparity between the sexes. As far as age is concerned, generally speaking, cases of the rheumatoid type are seen oftener at an age approaching 40 than at 20, and I have also had one female aged 78 and one male aged 74. I have noted that the more acute cases tend to occur in subjects of asthenic build, associated with marked wasting, the characteristic textbook description. The more insidious cases tend to occur in the higher age-groups; they may sometimes be quite robust, and I believe the 20 to 40 age-period of the textbooks requires a degree of modification. In my series only a few cases of the osteo-arthritic type have occurred before the age of 40; the age-period 40 to 60 and beyond of the textbooks is in keeping with clinical experience. The age-period in the non-articular group is very variable since this type may be primary, or secondary to another group.

Posture and body build.—Broadly speaking the tendency would seem to be for the younger rheumatoid subject (particularly where the onset is acute or subacute) to be of asthenic build while the older victim of degenerative joint disease is more often of robust hypersthenic build. Few patients have a perfect posture: of the thin narrow-chested individuals Osgood has said "their muscles are poor, their thoracic cages are narrowed, their diaphragmatic excursion is small, their abdominal viscera are sagged, the weight-bearing lines of their joints are not true, muscle tone is hard to maintain because the centre of gravity is disturbed". In the osteo-arthritic hypersthenic build postural disturbance with dorsal kyphosis and lumbar lordosis and abdominal sag are by no means uncommon. Obesity with its traumatizing factor contributes to postural disturbance and the mechanical strain on weight-bearing areas has a marked repercussion on the locomotor system. In every case the body posture, standing and on locomotion, should be noted as a routine measure.

Hereditary predisposition.—In a series of 100 cases of the rheumatoid type of arthritis I found that 20 had a significant family history. The ætiological significance of a genetically inherited predisposition is noteworthy (both mentally and physically). To cite two recent cases: two sisters suffering from a rheumatoid type of arthritis have the disease localized in the knee-joints while a third sister has died of rheumatic carditis. Another female patient, aged 50, with the rheumatoid type of arthritis, has been nursing a crippled sister with advanced rheumatoid arthritis for four and a half years, and a younger brother has rheumatoid arthritis. This constitutional susceptibility to disease is evident from the many reported instances of identical disease occurring in identical twins. Recognition of the underlying constitutional factors (inherent inferior joint tissues, impaired blood supply, body build, &c.) with the determining mechanism of varying susceptibility in the individual patient is secondary only in importance to external environmental factors.

Autonomic imbalance.—The conception of an autonomic nervous imbalance preceding by many years the onset of the disease is receiving growing recognition. Moreover, the psychogenic make-up of the patient may be intimately linked to the constitutional factor. Mitchell and I (1936), in studying a group of patients with chronic arthritis at the Order of St. John Clinic for Rheumatism, were impressed by the tendency towards morbid anxiety in many of the rheumatoid type, both prior to and following the onset of the disease. They were obviously more sensitive than usual to worry and emotional stress. An evaluation of the patient's psychogenic make-up in facilitating the onset of the disease, in impeding recovery, and in increasing the relapse incidence is important, although many observers have stated that subjects of degenerative joint disease are, on the whole, more placid and stable. This was contrary to our own experience, although genetic studies reinforced the view that the previous personality make-up largely predisposed the type of mental state following the illness. The relationship of mental states to physical dysfunction (i.e. the importance of endocrine autonomic dysfunction), and even to anaphylactic shock and the like have been described. It might be asked whether mental disturbance leads to organic disease in the arthritic subject. Our studies, as far as they went, did not permit a definite answer to this question. It seems likely, however, that both mental disturbance and organic disease are evidence of a general biological inadequacy.

Trauma.—With regard to degenerative joint disease a history of multiple minor or major physical traumata is often revealed, in contrast to the psychogenic traumata of the rheumatoid group but, as I have already stated, it is not the only precipitating factor. The inherent tendency to this form of arthritis is illustrated by the frequent incidence of the same condition in members of the same family. In such circumstances, with inferior cartilaginous and bone structure, the degenerative influence of trauma can be readily appreciated. Furthermore, disturbed body postures, obesity and occupational trauma, endocrine and metabolic factors may all aggravate the degenerative process. Senescence alone cannot be regarded as a causative agent having regard to those who, by reason, perhaps, of an inherited relative immunity, escape the disease.

Non-articular rheumatism.—Finally, I must refer to non-articular rheumatism, the so-called fibrositis. This condition has a symptom complex which includes pain, stiffness, and limitation of movement which can occur as a manifestation of psychoneurotic illness. The term was orginally introduced by Garrod in 1904 and has since been applied to so many maladies differing in ætiology and pathology but sharing a common symptomatology that some American workers have asked whether fibrositis does, in fact, exist as a clinical entity. Broadly speaking, however, a clinical definition of fibrositis would be an acute, subacute, or chronic non-suppurative condition characterized by pain and stiffness, especially on movement, affecting the fibrous origins, insertions, and aponeuroses of muscles, subcutaneous and deep fascia, ligaments, tendons, supporting tissues of certain nerves, and fibrous portions of joint capsules. The primary form of fibrositis is unaccompanied by any other recognized disease, while the secondary form it may also take may be an accompanying process in rheumatic fever, the rheumatoid and osteo-arthritic types of chronic arthritis, gout, certain pyrexial illnesses, &c. Since the ætiology is unknown such factors as occupation, climate, exposure to damp and cold, trauma and fatigue (mental or physical), diet, postural disturbance, metabolic, endocrine, microbic and focal infection may singly or jointly be significant. Time will only permit me to refer briefly to certain biographical studies which my colleagues and I have made during the war on civilian and military sufferers of so-called fibrositis at a Rheumatism Unit at St. Stephen's Hospital and at the Leatherhead Emergency Hospital, studies considerably extended since our original report published in 1942. I would like to preface these remarks by a few observations on Halliday's studies of insured persons who had been certified as unfit for work by reason of non-articular rheumatism. He emphasized that at least 40% were, in fact, incapacitated not by rheumatism but by psychoneurotic illness. Psychogenic muscular pain as an outward manifestation of acute or chronic emotional disturbance, causing autonomic disturbances and vascular instability with ischæmia or muscle spasm, is well recognized. We ourselves have been struck with the association of physical disablement and emotional psychoneurotic disturbances in cases of fleeting bodily pains which have not responded to several months of routine treatment. Of 50 cases labelled "fibrositis" all of whom had been ill for more than three months, we found (*Ann. rheum. Dis.* 1942) that 35 showed significant psychological disorders, 25 showing hysterical features, 7 suffering from anxiety states and 3 from depressive states. We noted a broad distinction between true and psychogenic fibrositis to the effect that in the organic form the pain was localized and could be reproduced by palpation, tension, contraction, or stretching in the affected area. The 35 psychogenic cases, on the other hand, complained of fleeting pains all over the body. In some cases of long-standing organic fibrositis the onset may well have been influenced by psychogenic factors which may also have exacerbated and prolonged the condition. It was, however, particularly noteworthy that psychological abnormalities were absent even in cases of long standing where the complaint could be sufficiently explained by gross structural lesions.

In psychogenic fibrositis the muscles serve as defence and attack in the struggle for existence and internal tension is most easily released by muscular action. Hence, if the external expression of aggressiveness in the form of muscular action is inhibited by repressing forces operative in the individual, muscular tension may result and is felt by the individual as pain and limitation of movement. This is commonly interpreted as fibrositis but I feel that the subject is at least comparable in importance to the so-called effort syndrome. This is now generally recognized as a psychoneurotic disability with a physical manifestation in the cardiovascular system, whereas the basis of certain so-called rheumatic pains is manifested physically in the locomotor system. Our work has received adequate confirmation by Flynd and Stuart Barber studying certain R.A.F. personnel.

It is often difficult to differentiate organic from psychogenic fibrositis but the following criteria, although not foolproof, are helpful:

(1) Pain and local tenderness.

(2) Reproduction of symptoms by pressure on tender focal points.

(3) Presence of nodules (which may be painful or painless). It should be noted that nodules are not infrequently felt in the course of routine examinations in subjects who are quite free from symptoms.

(4) The relief of symptoms on injections of novocain into trigger areas.

It must, however, be recognized that pain of a prolapsed disc, for example, or a spinal tumour with reflex lumbar spasm simulating lumbar fibrositis may be partially relieved by novocain infiltration.

SUMMARY

(1) The problem of the ætiology of the chronic rheumatic diseases with their wide systemic and local manifestations is essentially one for the general physician with a special interest in this sphere, and the general practitioner in consultation with a team of expert colleagues.

(2) The influence of various ætiological factors has been briefly assessed and reviewed.

(3) The development of ætiology in relation to environmental studies (biological, physical, occupational, and mental) and socio-medical investigations has been emphasized.

(4) A complete rheumatism service, visualized in the National Health Service, comprehends specialized rheumatism units, suitably placed according to the needs of the population, a plan analogous to the proposed tuberculosis and chest service. These units should, wherever possible, be centred in the atmosphere of a general teaching hospital with all its available ancillary services, linked also to an adequate number of beds in country hospitals run on sanatorium lines. In such institutions under- and post-graduate teaching, co-ordinated research as well as treatment should be their primary function. In this way more favourable conditions for

progress in relation to ætiology with consequent advances in the control and treatment of this widespread scourge would be made more effective.

BIBLIOGRAPHY

ANGEVINE, D. M., ROTHBARD, S., and CECIL, R. L. (1940) *J. Amer. med. Ass.*, **115**, 2112.
BAGENSTROSS, A. H., and ROSENBERG, E. F. (1941) *Proc. Mayo. Clin.*, 16, 232.
BAYLES, T. B. (1943) *Amer. J. med. Sci.*, **42**, 205.
BONNEY, V. (1943) *Lancet* (ii), 669.
COHEN, HENRY (1943) The Nature's Methods and Purpose of Diagnosis. The Skinner Lecture. *Lancet* (i), 23.
DAVIDSON, L. S. P. (1944) The Etiology of Chronic Rheumatism. Glasgow.
DAVIDSON, MAURICE (1946) *Post. Grad. med. J.*, **22**, 379.
EAGLES, G. H., EVANS, P. R., FISHER, A. G. T., and KEITH, J. D. (1937) *Lancet* (ii), 421.
ELLMAN, PHILIP (1944) *Lancet* (ii), 581.
——, and MITCHELL, S. D. (1936) *Rep. Chron. Rheumat. Dis.*, **2**, 109.
——, SAVAGE, O. A., WITTKOWER, E., ROGERS, T. F. (1942) *Ann. rheum. Dis.*, **3**, 56.
FLYND, J., and BARBER, H. S. (1945) *Quart. J. Med.*, **14**, 57.
FRIED, B. M. (1943) *Arch. int. Med.*, **72**, 565.
GARROD, A. E. (1905-6) *Trans. med. Soc. Lond.*, **29**, 94.
GRANIRER, L. W. (1946, May) *Med. Clin. N. Amer.*, **30**, 562, 645.
HENCH, P. S. (1938) *Proc. Mayo. Clin.*, **13**, 161.
——, and ROSENBERG, E. F. (1944) *Arch. int. Med.*, **73**, 293.
HUTCHINSON, J. (1881) *Med. Times, Lond.* (ii), 757.
LEVINTHAL, W. M. (1943) *Edinb. med. J.*, **50**, 415.
OSGOOD, R. B. (1938) Survey of Chronic Rheumatic Diseases. Ed. R. G. GORDON. London. 277.
RICH, A. R. (1943) *Bull. Johns Hopk. Hosp.*, **73**, 239.
RYLE, J. A. (1947) *Lancet* (i), 1.
SABIN, A. B. (1939) *Science*, **89**, 228.
SCHLESINGER, B. (1938) Survey of Chronic Rheumatic Diseases. Ed. R. G. GORDON. London. 201.
SELYE, H. (1944) *J. Amer. med. Ass.*, **124**, 201.
URBACH, E. (1944) *J. Amer. med. Ass.*, **124**, 731.
WEBER, F. P. (1946) *Lancet* (ii), 931.
YOUNG, D., and SCHWEDEL, T. B. (1944) *Amer. Heart. J.*, **28**, 1.

(This Paper was illustrated by many clinical and X-ray photographs.)

Dr. G. D. Kersley: If osteo-arthritis is excluded from the discussion, the remainder of the rheumatic syndromes have certain points in common. They are all affections involving any or all of the mesodermal structures of the body and no others. All may apparently be caused by, or an attack be initiated by, a large number of common factors. In none of the syndromes has a specific infection been proven, though they are liable to occur during or after nearly any infection.

The only theory of ætiology which appears to cover the known facts is that rheumatism is caused by "an altered reaction of the macro-organism to an invasion by a foreign protein". Such a theory immediately raises four questions:

What is the altered reaction and what evidence is there that such a state exists; how can it be brought about and what are the foreign proteins which may be responsible?

(1) Supposing the altered reaction be classified as a type of sensitization, what does this necessitate immunologically? Sensitization is "a state of potential toxicity due to an intracellular antigen-antibody reaction". For this reaction to occur there are two requisites, namely, cell-fixed antibody and insufficient circulating antibody to neutralize the antigen.

(2) What evidence is there to suggest that such a state of sensitization occurs in rheumatism?

(*a*) Experimentally it has been shown (Roessle, 1936) that the local tissue reaction in sensitized animals is mesodermal only and resembles in many ways the rheumatic granuloma. Moreover, the reaction may be localized to a particular area by hyperæmia, trauma or fatigue (Klinge, 1929), frequent factors concerned in localizing rheumatic and gouty phenomena.

(*b*) Rheumatic pains frequently occur during the course of scarlet fever immunization (Rhoads and Afremow, 1943).

(*c*) When rheumatism develops as the apparent result of an infection there is usually a lag or incubation or sensitizing period of some two weeks between the onset of the infection and the first rheumatic symptoms.

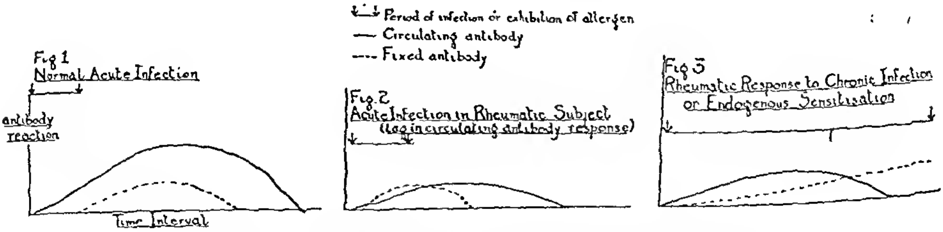
(*d*) Abnormally slow immune body response has been shown to occur when rheumatic subjects are infected with the hæmolytic streptococcus (Coburn and Pauli, 1939) and a similar slow response was suggested by Levinthal's work (1939) with yeast vaccines in rheumatoid patients.

(*e*) The response of some rheumatic conditions to salicylates and the absence of their response to sulphonamides or penicillin, except in long-continued prophylactic doses, can again be used as suggestive evidence in favour of a sensitivity factor in the rheumatic state.

(3) What factors may contribute in producing a susceptibility to sensitization? There may be a hereditary predisposition, best seen perhaps in gout and also in rheumatic fever, where Wilson suggests a mendelian factor is concerned. Alternatively, immunity, i.e. the presence of antibody in the blood-stream, may be depressed both by chronic infection, fatigue, exposure and climatic conditions and also by upset of the autonomic nervous system due to worry or shock—all common factors in initiating or aggravating the rheumatic state.

(4) What are the foreign proteins that may become antigenic in this sensitivity reaction? They may be exogenous in the shape of bacteria or their products, certain foods or even drugs (e.g. the sulphonamides) or in some cases they may perhaps be endogenous products liberated by physical microtraumata. Instances of the latter are chills, excessive fatigue and the repeated traumata which at first produce a monarticular arthritis. The arthritis may suddenly spread to many joints, taking on the character of a typical polyarthritis. The effect of such allergens is best exemplified and studied in the clear-cut attacks occurring in gout.

In the normal individual the response to infection consists of the production of antibodies in the serum before and in excess of any cell-fixed antibody (fig. 1). In "rheumatism" caused by acute infection or by a food or drug allergy, it is suggested that the serum antibody response is slow (Coburn and Pauli, Levinthal) so that, for a time, cell-fixed antibodies come into play causing an acute attack of arthritis or fibrositis (fig. 2). With a chronic infection or endogenous sensitization the immune body response may gradually become depressed so that the serum antibodies fall off, uncovering those that are fixed intracellularly, thus producing a chronic rheumatic state (fig. 3).



Fixed and circulating antibody curves resulting from an infection.

The above state of affairs, though to some extent hypothetical, does suggest certain obvious lines for further research and, possibly later, for treatment.

BIBLIOGRAPHY

Coburn, A. F., and Pauli, R. H. (1939) *J. clin. Invest.*, **18**, 147.
Klinge, F. (1929) *Beitr. path. Anat.*, **83**, 185.
Levinthal, W. (1939) *Ann. rheum. Dis.*, **1**, 67.
Rhoads, P. S., and Afremow, M. L. (1943) *Ann. intern. Med.*, **19**, 60.
Roessle, R. (1936) *Acta rheum.*, *Amst.*, **8**, 29, 1.
Wilson, M. G. (1944) *J. Amer. med. Ass.*, **124**, 1188.

Dr. Ernest Fletcher stressed the point that rheumatic fever and rheumatoid arthritis may be extremely difficult to separate clinically and related a case in which it had been impossible to do so until the case came to autopsy.

With regard to the question of allergy in chronic rheumatism, he mentioned Cooke's recent work in which he described two types of clinical allergy, the "immediate" and the "delayed" type. In the immediate type the skin test becomes positive very rapidly and a passive transfer of skin-sensitizing antibodies occurs, i.e. Prausnitz-Kustner phenomenon is present.

The delayed type has a fairly constant incubation period but the skin test is negative and passive transference does not occur. Confusion between these two types has led to the use, and abuse, of skin tests and a good deal of error.

With regard to focal sepsis, the figures were very variable throughout the world but in a series of 254 cases of rheumatoid arthritis and 253 cases of osteo-arthritis, the percentage of cases rendered symptom free at the end of five years was 2·3 and 0·3.

Dr. W. R. Thrower said that he welcomed Dr. Kersley's contribution to the discussion because it was a real attempt to obtain an understanding of the essential pathology of rheumatism which for so long had been influenced by dogma and loose thinking. The fact that Dr. Kersley had suggested that rheumatic disorders were essentially a disturbance in mesoblastic structures was very reasonable when it was remembered that other embryological systems of the body had their own peculiar disorders, brought about usually by microbes which had a predilection for them. For instance, epiblastic structures were principally attacked by coccal infections and hypoblastic structures by bacillary infections. A reactive phase due to allergy or allied conditions might well occur in the mesoblastic system, the clinical features depending on which part was primarily involved. In the other disorders mentioned, localized manifestations often appeared, but the basic principle remained.

He hoped that this new concept of the rheumatic disorders might serve at least as a basis for a better understanding of the fundamental pathology of rheumatism to replace the numerous explanations now offered. It was only after a true appreciation of the cause of rheumatism that satisfactory control and treatment would be possible.

Dr. W. Annandale Troup: In my opinion one of the commonest causes of rheumatism in its various manifestations is chronic nasal catarrh and sinusitis. The profession as a whole quite erroneously informs the patient that there is no cure for these conditions and the patient drifts on from year to year using nasal drops and solutions in atomizers. Chronic nasal catarrh and sinusitis can be alleviated and cured by physical methods of treatment. By this I mean treatment by means of the Kromayer mercury vapour lamp and adjuvant physical methods. Over the last twenty years I have treated a great number of such cases. One invariably notes that the secondary toxæmic manifestations of rheumatism, which are invariably present in cases of long standing, subside and in the majority of cases disappear as the result of the successful treatment of the primary focus.

Operations for sinusitis, particularly if repeated, almost invariably lead to a lighting up of the rheumatic symptoms. The late Mr. Watson-Williams in his book "Chronic Nasal Sinusitis and its Relation to General Medicine" devotes several pages to chronic nasal sinusitis as an ætiological factor in the causation of various forms of rheumatism. Intestinal toxæmia, so frequently cited as a cause of rheumatism, is treated, but the chronic nasal catarrh which in many cases causes this is left untouched. Again, infected tonsils may be removed but the chronic catarrh which caused the infection is left untouched.

The enlightened treatment of chronic nasal catarrh and sinusitis would result in a marked reduction of the incidence of rheumatism.

Dr. W. Ganado: In brucellosis there is a very high incidence of arthritis, towards the end of the disease; indeed its occurrence before the sixth week is a rarity. This time-interval has suggested that sensitization is the cause of the arthritis, but the serum agglutinins are still at a high titre even when the arthritis occurs. It is possible that the antigen(s) causing the arthritis is different from the antigen producing agglutination. To argue from analogy is always unsafe especially when other presumptions are also involved. It is suggested that investigations on the ætiology of chronic rheumatism should include investigation for antigens that give other tests apart from agglutination.

ADDENDUM

SECTION OF MEDICINE—MEETING ON NOVEMBER 26, 1946

Discussion: "Birth Control: Some Medical and Legal Aspects"

The following paragraph was unavoidably omitted from the report of the Discussion in the *Proceedings* for December 1946, page 51, vol. 40.

Dr. Eustace Chesser: It is a disconcerting fact that doctors seem unable to consider, far less discuss, sex and contraceptive technique without their views being highly coloured by their own emotional make-up.

Mr. Green-Armytage has given us a very good example of "wishful thinking" when he states that in many Centres in the country, young girls are fitted with birth control "gadgets". Surely, he must be aware that nothing could be further from the truth.

Mr. Aleck Bourne is obviously not immune from this emotional bias—to wit his criticism of the Gräfenberg or silver ring. For example, what evidence has he for asserting that the ring acts as an abortifacient? Particularly when he himself states that he has delivered two women of full-term babies with the ring *in utero*?

What evidence has he for stating that the ring *per se* can produce a salpingitis? Surely, he must appreciate that such an infection can only be resultant on the *operation for the insertion of the ring.* If this is done with skilled hands, and under proper aseptic conditions, the risk of infection is certainly no greater than that following any minor operative procedure.

I think it is time it was realized that contraceptive technique is not merely a question of appliances or "gadgets"—but something much more subtle—personalities. In this mechanical age the latter fact has all too often been ignored.

Section of Experimental Medicine and Therapeutics

President—Professor H. P. HIMSWORTH, M.D.

[*January* 14, 1947]

Nutritional Liver Disease in West Indian Infants

By J. C. WATERLOW, M.B.

A DISEASE occurs among babies in the West Indies, whose main features are œdema, gross muscular wasting, and fatty infiltration of the liver. The onset is usually in the second six months of life, within three months of weaning. The presenting symptoms are vomiting and œdema. The œdema is of the hypoproteinæmic type, without albuminuria. The mortality of the disease is high and death appears to be due to hepatic failure. Analysis of the liver in fatal cases shows a fat content of up to 50% of the fresh weight. Hepatic functional impairment may be demonstrated during life by the bromsulphalein test. Other liver function tests, such as the colloidal gold test, and measurements of serum phosphatase, have given negative results. The presence of fatty infiltration can be confirmed by histological examination of liver tissue removed by aspiration biopsy.

This syndrome resembles closely the disease known in Africa as kwashiorkor, or infantile pellagra. In the African cases there are typically severe lesions of the skin and mucocutaneous junctions, and depigmentation of the hair—changes attributable to deficiency of riboflavin and of other members of the vitamin B_2 complex. The condition has generally been looked upon as the result of a mixed deficiency of protein and of B vitamins, and it has been suggested that the fatty liver is a manifestation of pellagra (Gillman and Gillman, 1945*a*) or of ariboflavinosis (Hughes, 1946). However, in the West Indian babies lesions of the skin, hair and mucosæ were seldom severe and were sometimes absent. In no case would the diagnosis of infantile pellagra be appropriate. In spite of this, the condition, judged by the mortality rate and by the degree of fatty infiltration of the liver, was no less severe than in Africa. This suggests that fatty liver in infants should be regarded as a disease *sui generis*, which may or may not be associated with signs of vitamin deficiency. For simplicity's sake it will be called the "fatty liver disease".

Certain objections have to be met before fatty liver in infants can be accepted as a specific entity. It is well known that severe fatty infiltration of the liver is found in infants dying of conditions such as gastro-enteritis or bronchopneumonia. But although the end-result may be the same in gastro-enteritis and in fatty liver disease, there may be a difference in the mechanism by which the fat accumulates in the liver. It is probable that in wasting diseases and in infections the fat in the liver is endogenous, derived from the body stores. It is suggested that in fatty liver disease the fat is exogenous, derived from the food. There is typically a history of feeding on a diet consisting mainly of starchy foods, low in protein and vitamins but with a high calorific value. Moreover, even in severe cases the fat depots are not entirely depleted; considerable quantities of subcutaneous fat are found at post-mortem. It is of interest that in the condition described by the German pædiatricians as "Mehlnährschaden" and attributed to overfeeding with carbohydrate, an intensely fatty liver has been observed (Huebschmann, 1921; Saito, 1924).

Overloading with calories is only one factor in producing fatty liver in these babies. It is generally agreed, and the evidence is very strong, that the underlying cause is a dietary deficiency of some kind. Experimentally the most widely studied type of dietary fatty liver is that produced by choline deficiency. The effects of choline deficiency can be prevented by methionine, which acts as a source of labile methyl groups. Inositol has a lipotropic action which is synergistic to that of choline. However, in babies with fatty liver, in the small number of cases tested in the West Indies, neither choline, methionine nor inositol appeared to have any effect in improving the condition of the liver or in saving life. Vitamin B_1, riboflavin, and nicotinic acid have been tried by workers in Africa with equally unsatisfactory results. On the other hand, good results have been obtained by the use of crude substances. Gillman and Gillman (1945*b*) in Johannesburg reported an excellent response to dried stomach. This has been both confirmed and denied (Trowell, 1946; Gelfand, 1946). In the West Indies it was found that a striking improvement occurred with no other treatment than an increased intake in milk. These results were controlled as far as possible by placing cases on a low milk intake for a preliminary period. On an intake of 7 to 8 oz. daily the condition remained more or less stationary; when the intake was increased to 30 oz. there was a rapid loss of œdema, a rise in serum protein concentration, and in dye clearance, and a more gradual decrease in the size of the liver. Serial biopsies showed a concomitant decrease in the severity of the fatty infiltration. No comparison is available between the effects of milk and of dried stomach. Our effort was directed to obtaining a base-line for the effects of milk alone, because all practical diets for babies must contain some milk. Until its action is known, it is impossible to investigate accurately the effectiveness of other substances. There is an urgent need for systematic fractionation and assay of the crude materials found effective. The isolation of an active substance which could be given parenterally would undoubtedly save many lives, since in severe cases oral treatment is made difficult by persistent vomiting.

All the evidence—the history, the associated lesions (hypoproteinæmic œdema and dermal and mucosal changes) and the response to treatment—suggests that the underlying deficiency in this fatty liver disease is either of protein or of some member of the vitamin B_2 complex; but it is not yet possible to choose between these alternatives. Reasons have already been given to suggest that neither riboflavin nor nicotinic acid is involved. Little is known about the possible rôle of the other B vitamins, apart from choline and inositol: but it is significant that good results in treatment have not been obtained with yeast. On the other hand, œdema is very constant in severe cases. There is gross macroscopic and microscopic wasting of muscles. Analyses of the liver in five fatal cases show a 20% decrease in the non-fatty solids, which are mainly protein. There is thus evidence of depletion in the three most important protein reservoirs of the body. Recent work on dogs (Fouts, 1943; Li and Freeman, 1946) has suggested a relation between protein deficiency and fatty liver. This type of fatty liver does not depend upon deficiency of methyl groups, since it is neither prevented nor cured by choline.

The cause of the fatty liver disease in infants is therefore still unknown. There is also much to be learnt about its natural history. In the course of the field investigations in the West Indies the question arose of how to recognize the disease in its early stages. In established cases that were responding successfully to treatment, it was found that the liver remains enlarged and, as shown by biopsy, still contains some fat for some time after the disappearance of the œdema and the restoration of normal serum protein concentration and dye clearance. It therefore seemed logical to suppose that in the development of the disease the reverse sequence occurs: that the first stage is a gradually increasing fatty infiltration and enlargement of the liver. Cases were found with enlargement of the liver but without other clinical or biochemical abnormalities, and with no evidence of malaria or syphilis. Biopsy of the liver in two such cases showed a moderate degree of fat, which was much decreased after one week on a high milk intake. This response to improved diet suggests that, in spite of the good clinical condition of the babies, fatty infiltration of the liver cannot be regarded as normal. It seems probable that such infants represent early or larval cases of the fatty liver disease, many of which become spontaneously cured. Babies with symptomless enlargement of the liver were common in the West Indies: they were more common in the second than in the first six months of life, which suggests that the enlargement was not merely an exaggeration of the physiological condition of the liver in the newborn.

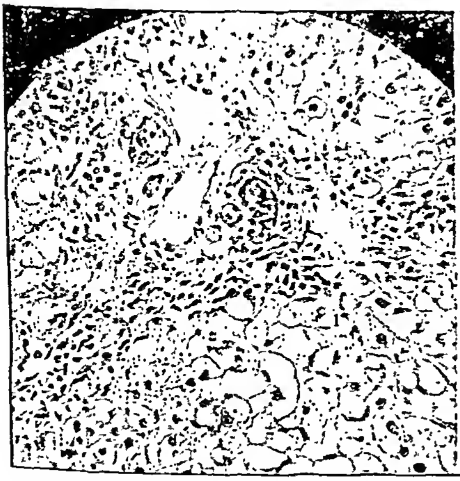


FIG. 1.

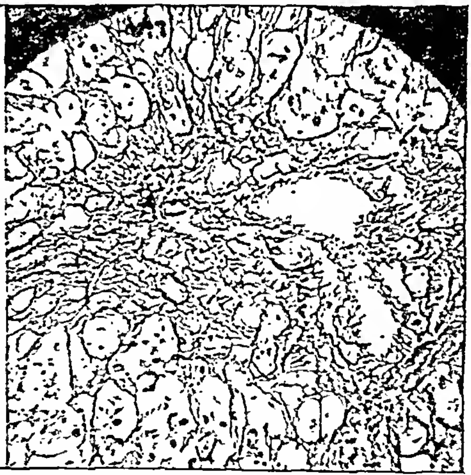


FIG. 2.

FIG. 1.—Liver. Biopsy specimen. Hæmatoxylin and eosin. × 187. There is cellular infiltration of the portal tract, and an increase of connective tissue. The liver contained no fat at the time that this biopsy was taken. The vesicular appearance of the hepatic cells is caused by the presence of glycogen. This specimen was taken from an infant aged 16 months, with enlargement of the liver, reduced hepatic function, œdema, and ascites.

FIG. 2.—As fig. 1. Silver impregnation (Gömöri's method) × 187. There is an increase of silver-staining fibres in the portal tract, and an outgrowth of fibres into the parenchyma, to form a fine network, surrounding some liver cells at the edges of the lobules.

In the age-group 6 to 18 months, definite enlargement of the liver (liver edge one fingerbreadth or more below the costal margin), not associated with signs of syphilis or enlargement of the spleen, was found in 10% of unselected infants. If the hypothesis outlined above is correct, then the fatty liver disease, at any rate in mild grades, must be regarded as a common condition in the West Indies. From the practical point of view, as regards prevention and treatment in infant welfare clinics, it might be said that enlargement of the liver without enlargement of the spleen is an indication for a supply of extra milk.

Finally, there is evidence that there may be late sequelæ in cases which neither die nor recover completely. In Jamaica cirrhosis of the liver in childhood is not uncommon. A series of cases was described by McFarlane and Branday (1945) with an average age of 5 years. Experimentally it has been shown both in rats (Lillie *et al.*, 1942) and in dogs (Chaikoff *et al.*, 1938) that fatty infiltration of the liver may proceed to cirrhosis. In human pathology, a similar sequence has been described in diabetes and in chronic alcoholism (Connor, 1938). It therefore seemed probable that cirrhosis of the liver in children in the West Indies might be the result of preceding fatty infiltration in infancy. An attempt was made to collect by means of liver biopsy pathological material to demonstrate this sequence of events. This material is as yet far from complete. The earliest change that has been seen is a thickening of the portal tracts, with round-cell infiltration and some proliferation of fibrocytes. This has been found in an infant 1 year old with a fatty liver of at least three months' standing. The next stage appears to be an outgrowth of reticulin fibres into the parenchyma from the portal tracts; these fibres penetrate between the hepatic cells at the edge of the lobule, and surround them. This has been seen in a child of 16 months (figs. 1 and 2). At a still later stage, some of the ingrowing fibres develop the histological characteristics of collagen, forming bands traversing the liver lobule. At this point the normal architecture of the liver begins to be destroyed. This pathological picture has been found in a child of 18 months with signs of portal destruction.

In rats, Himsworth and Glynn (1944) have described two types of dietary cirrhosis: in the first the fibrosis is diffuse, follows fatty infiltration and is caused by choline deficiency; in the second the fibrosis is coarse, follows massive necrosis, and is caused by deficiency of sulphur-amino-acids. In the infants described, the fibrosis was diffuse, with no sign of necrosis; there is therefore no resemblance to the second of the two sequences in the rat, and no reason to look upon sulphur-amino-acid deficiency as a possible cause.

Cirrhosis of the liver is much commoner in tropical than in temperate countries, with a high incidence in the fourth decade of life. Reports from all parts of the world show that this cirrhosis is predominantly of the diffuse Laennec type, often accompanied by fat. There is at present no evidence that "tropical cirrhosis" is a dietary disease: but the sequence of events that has been described in infants and children in the West Indies, which leads to an identical pathological picture may help to throw some light on its pathogenesis and cause.

The suggestions put forward in this paper are based on the preliminary findings in a small number of cases, and are therefore to be regarded as tentative, until supported by further evidence.

ACKNOWLEDGMENT

I am deeply indebted to the Directors of Medical Services in Trinidad, British Guiana and Jamaica for giving me facilities to work, and to numerous others in all three colonies for encouragement and help.

REFERENCES
Chaikoff, K. L., Connor, C. L., and Biskmol, G. R. (1938) *Amer. J. Path.*, 14, 101.
Connor, C. L. (1938) *Amer. J. Path.*, 14, 347.
Fouts, P. (1943) *J. Nutrit.*, 25, 217.
Gelfand, M. (1946) *Clin. Proc.*, 5, 135.
Gillman, T., and Gillman, J. (1945*a*) *Arch. Path. Lab. Med.*, 40, 239.
——, —— (1945*b*) *Arch. intern. Med.*, 76, 63.
Himsworth, H. P., and Glynn, L. E. (1944) *Clin. Sci.*, 5, 93.
Huebschmann, P. (1921) *Verh. dtsch. path. Ges.*, 18, 216.
Hughes, W. (1946) *Trans. R. Soc. trop. Med. Hyg.*, 39, 437.
Li, T. W., and Freeman, S. (1946) *Amer. J. Physiol.*, 145, 646.
Lillie, R. D., Ashburn, L. L., Sebrell, W. M., Daft, F. S., and Lowry, J. V. (1942) *Pub. Hlth. Rep., Wash.*, 57, 502.
McFarlane, A. L., and Branday, W. J. (1945) *Brit. med. J.*, (i), 838.
Saito, M. (1924) *Virchows Arch.*, 250, 69.
Trowell, H. C. (1946) *E. Afr. med. J.*, 23, 34.

Dr. P. Ellinger: I fully agree with Dr. Waterlow that the condition he has described has nothing to do with real pellagra and I regret that by some authors it has been called infantile pellagra. Amongst hundreds of pellagra cases which I saw in Egypt in 1937 and 1938, as far as I can remember, there were no children below 4, the critical age of the nutritional liver disease. I examined in numerous villages of the Delta parts of the population selected at random. Amongst the people examined were numerous small children below 4 all of whom were free but pellagra was very frequent amongst children between 4 and 10 years.

I was also allowed to examine the post-mortem reports of the Department of Pathology of the Faculty of Medicine of the University of Cairo for reports on pellagrins. They were not very numerous but I could not find any remark on liver damage found in these pellagra post-mortems.

Some Renal Effects of Experimental Dietary Deficiencies

By H. Heller, M.B., Ph.D., and S. E. Dicker, M.D.

Dr. H. Heller: Liver lesions may be produced experimentally by feeding protein-deficient diets and it has been recently suggested (Himsworth and Glynn, 1944) that hepatic poisons act ultimately by reducing the supply of protective protein derivatives to the liver. Now many of the toxic factors which produce liver damage also give rise to lesions of the kidneys. The question arose, therefore, whether chronic protein deficiency may damage the kidney as well as the liver.

Following this idea it was decided to investigate the kidneys and the water metabolism of animals fed on various protein-deficient diets. The diet first used was modelled on the type of food which, in concentration and prison camps, has frequently been reported to lead to hypoproteinæmia and œdema, namely a protein-deficient vegetable diet of low calorific value. The supply of this diet which consisted essentially of raw turnips, starch, fat and adequate amounts of vitamins, was not restricted but its calorie value was so low that the amount eaten per animal per twenty-four hours provided only one-third of the number of calories supplied by the control diet. Other rats received a diet of the same composition but with fresh carrots taking the place of fresh turnips. These diets, while containing less than 0·9% of vegetable protein, contained sufficient amounts of choline to eliminate a deficiency of that substance.

Adult rats fed on the protein-deficient vegetable diets lost weight rapidly (about 35% of the initial body-weight in forty days). The mean plasma protein level fell from 7·6 to 4·7 grammes/100 c.c. in the same time. Externally there was little amiss. There was no diarrhœa. A sudden increase in body-weight occurring after a period of steady loss of weight was interpreted as due to accumulation of œdema fluid. The presence of ascites was subsequently verified in some of these animals. Ascites could also be frequently induced by giving 5% of the animal's weight of water by stomach tube. Diuresis experiments showed that only about half of the normal amount of water was excreted in the urine, thus confirming this tendency to water retention. Measurements of urinary specific gravity showed moreover that rats on the protein-deficient vegetable diets, where given 5 c.c. water/100 g. body-weight, were unable to dilute the urine to the same degree as before the institution of the experimental diet. Nor could such animals, where deprived of water for twenty-four hours, concentrate the urine as efficiently as normally, suggesting the possibility of renal tubular impairment.

This simple method of investigation can hardly be said to yield unequivocal evidence as to the functional state of the kidney. However, the application of renal clearance methods gave the following picture of kidney function in the rats on the protein-deficient turnip diet: The *inulin clearance* (used as a measurement of the rate of glomerular filtration) was significantly higher than in normal animals. It bore no clear relation to the plasma protein level but was significantly correlated with the rate of urine flow. The latter finding suggests that the rise of the filtration rate was not due to an increased permeability of the glomerular capillaries. The absence of protein in the urine of rats on the protein-deficient turnip diet agrees with this. *Diodone clearances* at high plasma diodone levels showed a pronounced decrease of the rate of tubular diodone secretion in the majority of the rats on turnip diet. It is difficult to ascribe the lowered rate of diodone secretion to anything but an impairment of renal tubular function. This interpretation was also adopted by Earle, Taggart and Shannon (1944) who observed similarly low values for diodone secretion in cases of human chronic glomerulo-nephritis.

The lowered capacity for tubular diodone secretion was not the only pathological feature of the kidneys of rats on "turnip diet". Histologically demonstrable lesions were present in the kidneys of many of these animals and the same type of injury was found in many of the rats on "carrot diet". The lesions consisted of necrosis and calcification of the broad limb of Henle's loop, the glomeruli and other parts of the tubules showing no apparent changes. However, there was no correlation between the incidence or severity of the lesions and the results of the diodone clearance tests, which suggests that the two phenomena should be regarded as different pathological entities.

The histological picture seen in these kidneys was quite different from the hæmorrhagic lesions produced in very young rats by choline-deficient diets (Christensen, 1942; Engel and Salmon, 1941). However, it resembled markedly the lesions produced by feeding small amounts of racemic serine to rats on protein-deficient diets (Morehead, Fishman and Artom, 1944). The latter observation confirms older work on the nephrotoxic effect of certain amino-acids (Newburgh and Curtis, 1928; Cox, Smythe and Fishback, 1929). It seems of particular importance in suggesting that a protein-deficient diet may lead to a diminished resistance of the kidneys to the injurious effects of "nephrotoxic" substances. It may well be that a similar mechanism underlies the production of the renal lesions observed in our rats. A similar phenomenon is well known in connexion with hepatic injuries. For instance, Miller and Whipple (1940) have shown that the hepatotoxic action of chloroform increases as protein stores decrease.

The hypothesis that the low calorie turnip or carrot diet diminished the resistance of the kidney to the necrotizing action of some unknown constituent (a particular amino-acid for instance) contained in the vegetables may thus explain the occurrence of renal lesions in our rats but it is by no means the only possibility. It seems equally possible that the renal lesions occurred because the vegetable protein administered lacked one or several of the essential amino-acids. Or again they may have been due to the insufficient supply of protein as such and to the resulting severe hypoproteinæmia. Finally, the low calorific value of the experimental diets must not be forgotten. The accelerated breakdown of endogenous protein and the increased production of their metabolic end-products may not be irrelevant.

A series of rats were fed on a diet which contained only 0·5% of casein, i.e. approximately as little protein as the vegetable diets. However, the starch content of this diet was higher and the animals lost weight more slowly than the "turnip rats". Renal function tests were performed when the degree of hypoproteinæmia became comparable to that in the animals on the vegetable diets. They showed the following results: The rate of glomeruler filtration was comparable to that of the turnip rats in that it was raised and correlated with the urine flow. Diodone clearances showed in many cases a much decreased rate of tubular secretion, again the same finding as in the turnip animals. However, histological investigation of the kidneys failed to show the typical necrotic lesions. These findings suggest once more that the impairment of renal tubular secretion, found in both types of protein-deficient diets, is not related to the histological findings. (This lack of relationship is perhaps not very surprising considering the view of Smith and his school that diodone is secreted by the proximal tubules and considering that the necrotic lesions found in our rats were limited to the broad limb of Henle's loop.) The results obtained in the "low casein" series suggest further that the low plasma protein level, as such, was not the main determinant for the occurrence of renal lesions in the rats which had been fed on the vegetable diets. However, a relative deficiency of "essential" amino-acids in these animals has not been excluded. It is one of the ætiological factors which still await investigation.

REFERENCES

Christensen, K. (1942) *Arch. Path. Lab. Med.*, 34, 633.
Cox, G. J., Smythe, C. V., and Fishback, C. F. (1929) *J. biol. Chem.*, 82, 95.
Dicker, S. E., Heller, H., and Hewer, T. F. (1946) *Brit. J. exp. Path.*, 27, 158.
Earle, D. P., Taggart, J. V., and Shannon, J. A. (1944) *J. clin. Invest.*, 23, 119.
Engel, R. W., and Salmon, W. D. (1941) *J. Nutrit*, 22, 109.
Himsworth, H. P., and Glynn, L. E. (1944) *Lancet* (i), 457.
Miller, L. L., and Whipple, G. H. (1940) *Amer. J. med. Sci.*, 199, 204.
Morehead, R. P., Fishman, W. H., and Artom, C. (1944) *Amer. J. Path.*, 21, 803.
Newburgh, L. H., and Curtis, A. C. (1928) *Arch. intern. Med.*, 42, 801.

Dr. S. E. Dicker: Rats which had been fed on a protein-deficient vegetable diet for the same period and which had free access to water presented two different and contrasting pictures at post-mortem examination. Some animals had extremely "wet" tissues or even free liquid in the abdomen; others appeared abnormally "dry" with strikingly thin muscles. The decrease of the plasma protein level in the two groups was of the same magnitude. It was therefore thought of interest to examine whether, with reference to their water content, the tissues of the "dry" rats were essentially different from those of the rats with visible œdema.

When comparing the percentage of solids in plasma, muscle and liver of control rats with those of rats kept for sixty days on a vegetable diet, a significant decrease of solids in the tissues could be shown in both groups of the protein-deficient animals. The mean decrease of solids in the plasma amounted to 25·4%, that in the liver to 19·0%, but that in the muscle to 6·0% only. In other words, the increase in the total water content of muscle was much smaller than that in plasma or in the liver.

On the assumption that the cell membranes of rat muscle are impermeable to chloride, it is possible to calculate the extracellular fluid phase. By these means it could be estimated that the extracellular fluid phase of muscle of control rats amounted to a mean of 14·0 ml./100 grammes, that of the "dry" rats kept on the protein-deficient vegetable diet to 41·0 ml./100 grammes and that of the rats with visible œdema, fed on the same vegetable diet, to 55·0 ml./100 grammes.

It is thus clear that there was no essential difference between the two groups of hypoproteinæmic rats and that the "dry" animals suffered from occult œdema. It is therefore not surprising that the presence of visible œdema had no bearing on the outcome of the renal clearance tests.

[*February* 11, 1947]

DISCUSSION ON RADIOACTIVE TRACERS

Dr. A. S. McFarlane: One of the newer tools of physics about which much has been written in recent years is the cyclotron, a huge machine which whirls charged atoms around at ever-increasing speeds, and permits the physicist finally to hurl them at a target of his own choosing. If, as often happens, the whirling ion is that of deuterium, which has twice the mass of hydrogen, and the target is the metal beryllium, a radiation is given off by the beryllium which, like X-radiation, passes readily through the metal window of the cyclotron and has a powerful effect on a gold-leaf electroscope or on a photographic plate. Unlike X-radiation, however, it passes more readily through a sheet of lead than through a tank of water or a block of paraffin. This paradox—that more of the radiation gets through the denser medium—was resolved with many others by Sir James Chadwick when he showed that the beryllium radiates in fact a stream of uncharged particles each of virtually the same weight as a hydrogen atom and to which he gave the name neutrons.

If a piece of silver is held up to the stream of neutrons and is then taken into another room and brought near to an electroscope it will affect it much as did the original neutrons; it has in fact become radioactive. If the silver had been exposed instead to an X-ray beam it would have shown no radioactivity subsequently. The radioactivity of the silver does not remain constant but diminishes by half every two to three minutes so that after four to six minutes it is a quarter of the original value and after six to nine minutes one-eighth and so on. One might infer that the silver had stored up some neutrons and is giving them off again in its own time. However, the silver has little or no effect on the electroscope if a thin plate of metal is placed between the two, so clearly it is not giving off neutrons. It is not difficult to show that it is giving off electrons, the same light, negatively charged particles as are given off by radium. What has occurred is that each atom of silver, with a weight of 107 times the hydrogen atom, has captured one neutron so that its weight has increased to 108. Its chemical properties, however, are unchanged since these depend solely on the charge which of course is not affected by the acquisition of an uncharged particle. However, silver 108 is unstable and breaks down by giving off an electron of negligible weight. It therefore leaves behind cadmium 108 which has one positive charge more than silver. This is one example of a transmutation which takes place spontaneously as a result of our producing an unstable element.

It is, however, often quite easy to effect the transmutation directly by the action of neutrons. For example, if nitrogen in the form of an ammonium salt is exposed to the neutron beam it is converted into a radioactive form of carbon. It is an idiosyncrasy of the nitrogen atom, and of several others, that when it captures a neutron it does not feel at all happy and decides to throw out a hydrogen ion in exchange. The net result of this is to leave the atomic weight unchanged at 14, but a positive charge, which has been carried away by the hydrogen ion, is lost. Carbon 14 happens to have a half-life of 4,700 years—longer even than radium—and for this reason until recent years a visitor would observe around most cyclotrons, whatever they were being used for, a stack of bottles of ammonium nitrate set to catch stray neutrons. These would be left for months on end until a chemist came along and proceeded to extract a minute amount of carbon from all this salt, not demonstrably more than could be accounted for by the carbon impurity in the best grades of ammonium nitrate, but with radioactive properties.

To make the measurement of radioactivity more precise a device called a Geiger-Müller counter was developed and improved to such a degree that it will record the arrival of a single electron on a Post Office counter. There are some 10^{21}

atoms of silver in half a crown and when only one of these decides to change to cadmium the physicist can record the event with all the precision of a telephone call. The first samples of radioactive silver and carbon and other elements to be obtained were found to give out some hundreds of electrons per minute, corresponding to hundreds of atomic disintegrations per minute. However, bigger and better cyclotrons came along, followed by the uranium pile, which generates neutrons in fantastic quantities, and so the activities increased steadily until to-day samples of carbon are coming from the pile in one milligram of which one hundred million atoms of carbon disintegrate every minute. From a recent determination of the decay rate of carbon 14 by Reid and Dunning (1946) it is a simple matter to calculate that in one milligram of pure C^{14} rather more than ten thousand million atoms should disintegrate per minute, so that in these pile samples of carbon one part by weight in every hundred is the pure artificial element of atomic weight 14. There is no doubt that with further experience samples of 5% and even 10% purity will be available. But it is a relatively costly process and the present American price for 1 milligram of carbon containing about 10 micrograms of pure C^{14} is £100, which makes radium look comparatively cheap.

With some difficulty and the loss of at least half this valuable carbon an able chemist can prepare from it most of the metabolic substances in which we are interested containing a C^{14} atom in 1% of their molecules. Although an initial mg. of carbon gives off 10^8 electrons per minute in all directions it is only possible to collect a portion of these into the counter. In addition, since the electrons from carbon have very little energy some are absorbed by the counter window and altogether not much more than 10% of the electrons can be registered. Therefore, the count of the carbon in the substance prior to administration is found in practice to be reduced to about 5×10^6 per minute.

It is now known, largely as a result of isotope studies, that the body seldom makes use of exclusive metabolic pathways such as that by which iodine is built up only into the thyroid gland. Instead, most metabolic substances are attacked in a variety of highly specific ways affecting particular parts of the molecule. Amino groups are removed, carboxyl groups are oxidized and methyl groups are transferred from one substance to another, to give a few examples, and all at different rates. A group containing radio-carbon affected by one of these processes becomes mixed with the same group from molecules of other substances similarly affected, and the net result is that the specific radioactivity of the carbon in this group is reduced. If there are not many sources of the particular group the reduction will be small. In the worst case in which the carbon administered is in a hydrocarbon main chain it will be diluted with most of the carbon in the body. For an adult human being this means diluting our radio-carbon with roughly 5 kilos of tissue carbon, and if a 5 milligram sample of this is presented to the counter the C^{14} will show its presence by giving rise to 5 counts per minute, which is just about the lowest counting rate which is significant. If more than 5 milligrams of tissue carbon can be presented to the counter the accuracy will be proportionately greater. With laboratory animals a milligram of radio-carbon will clearly suffice for numerous experiments of this type. With humans the difficulty at present is that the safe dose of radio-carbon is not known with certainty, largely because of lack of knowledge of how long it persists in the tissues. As much as half a milligram of pure C^{14}, distributed uniformly throughout the body, may be permissible however.

If a sodium salt is placed in the neutron beam for a very short time and then presented to a counter it will give as many counts per minute as do the best samples of carbon. These counts come from sodium^{24} which has a half-life of only fourteen hours. The weight of pure Na^{42} present is immeasurable and yet we have an isotope preparation which will dilute as much as will 10 micrograms of pure C^{14} and still be detectable, because it disintegrates so quickly. Instead of costing £100 it is listed in America at a few shillings. It is detectable in a different way from C^{14} because in addition to electrons it emits (like radium) X-rays of the penetrating variety called γ-rays. It is possible, therefore, to measure the activity of Na^{24} with a sheet of metal in front of the counter or—of greater biological importance—with several centimetres of tissue between the source and the counter. Three minutes after drinking some radioactive sodium chloride it is sufficient to hold a hand in front of the counter and watch the rapid absorption into the blood-stream. This element when it becomes readily available should be of the greatest interest for measurements of the extra-cellular space and of electrolyte excretion.

Another -emitter is iodine^{131} of 8-days' half-life and costing three or four times as much as sodium. It can be detected in the thyroid by tucking the counter tube under the chin. This property is not possessed exclusively by γ-emitters. Some energetic electron emitters, e.g. radio-phosphorus, can be used for the same purpose, and Low-Beer (1946) claims to be able to detect local concentrations of radio-phosphorus in a breast carcinoma by superficial exploration with the counter. In general, however, the directional sense of the counters is poor on the one hand, and on the other the body seldom localizes elements with the degree of specificity which it shows towards iodine, phosphorus and calcium. A form of histochemistry is practised with the latter elements by placing a tissue section on a photographic plate, the radio-element revealing its position by causing a blackening of the plate.

Other radio-elements of potential or actual biological application are sulphur^{35} (half-life 88 days), chlorine^{36} (greater than 1,000 years), potassium^{42} (12 hours), calcium^{45} (180 days), iron^{55} (4 years) or ^{59} (47 days), arsenic^{76} (for use in toxicology and chemotherapeutics—26 hours), bromine^{80} (4½ hours), strontium^{85} (65 days), mercury^{197} (25 hours) or ^{203} (54 days), bismuth^{210} (5 days) and some very interesting inert gases for respiratory studies, e.g. argon^{41} (110 minutes) and xenon^{127} (34 days).

I would like to conclude with a brief reference to some important biochemical discoveries made with the use of isotopes. Twenty minutes after injecting subcutaneously a solution of sodium phosphate containing radioactive phosphorus the activity of the element in the plasma reaches a peak value and thereafter falls away very rapidly as the phosphate is taken up by the tissues. By giving diminishing quantities in spread injections it is possible to maintain an approximately constant level of radioactivity per milligram inorganic phosphorus in the plasma. During this period bone and other tissues, which take their phosphorus in inorganic form directly from the plasma, will receive phosphorus of constant specific activity and if the experiment goes on long enough the whole of the bone phosphorus will ultimately have this specific activity. For example rabbit epiphyseal bone phosphorus after seven weeks has an activity 30% of the plasma phosphorus showing that 30% of the bone phosphorus has been renewed in that time. By contrast one-quarter of the phospholipid in the liver is renewed in twelve hours (Hevesy and Hahn, 1940).

If we wish to know what proportion of the phosphorus in the fæces has been absorbed in the upper intestine and re-excreted in the lower it is only necessary to compare the specific radioactivity of fæcal phosphorus with that of the plasma or even the urine. The activity in the plasma is an equilibrium value determined by the rate at which inactive phosphorus arrives from the gut and radioactive from the injections. Phosphorus returned to the bowel comes from the plasma and must have the same specific activity before dilution with unabsorbed inactive phosphorus. The method is of course equally applicable to other dietary constituents.

This kind of work throws an altogether new light on the sites of formation in the body of many substances and on the speeds at which they are formed and broken down again. It reveals that the body is a complicated chemical factory, between constituent parts of which an incessant exchange of materials is taking place. This activity could not be suspected from the relatively desultory exchanges of food and excretory-products with the environment. Only by the use of elements chemically identical with the body elements, yet distinguishable physically, has it been possible to bring this to light.

REFERENCES

HEVESY, G., and HAHN, L. (1940) *Biol. Medd. Kbh.*, 15, Nr. 7.
LOW-BEER, B. V. A. (1946) *Science*, 104, 399.
REID, A. F., and DUNNING, J. R. (1946) *Physiol. Rev.*, 70, 431.

Dr. E. E. Pochin: Dr. McFarlane has given us a very clear and full account of what radioactive isotopes are, how they are produced and estimated, and what inferences may be drawn from their use in metabolic investigations. I wish now to discuss the types of problem to which they have been applied successfully. They have been used over a very wide field of work which has increased rapidly during the war, both in the United States and at Copenhagen and Stockholm. This work has hitherto concerned physiology rather more than medicine, and the illustrations which I will give are drawn commonly from this field. They show, however, how powerful and versatile is this technique of investigation, and how widely and readily it is applicable to clinical problems. I will also discuss briefly the therapeutic uses of these isotopes, although they are not strictly covered by our title, on account of the potential scope and interest of this field of experimental medicine.

We may consider first the simplest case, in which the fate of an administered chemical element is followed throughout its subsequent molecular combinations in the course of normal intermediary metabolism. It has been found, for example, that not only plants, but also animal tissues can utilize carbon dioxide in the formation of carbohydrate. For, if carbon dioxide is administered to an animal in which the carbon atom is radioactive, it is subsequently found that samples of glycogen from the body contain this radioactive carbon, and the path of its synthesis has been studied in this way through an initial condensation with pyruvic acid to oxalacetic acid and on to carbohydrate.

The same form of examination can be carried a step further by analysing the rate at which certain metabolic products are formed. For example, when radioactive iodine is added to thyroid tissue slices, the labelled iodine rapidly passes into combination as diiodotyrosine, and at the end of three hours is already present to the extent of 12% as thyroxine (Morton and Chaikoff, 1943). Similarly, iron administered by mouth has been detected in formed hæmoglobin in five hours (Pommerenke and others, 1942).

It is particularly valuable to be able to study the rates of reaction or formation of compounds, the concentration of which is ordinarily maintained in a state of stable equilibrium in the body. It has hitherto been difficult to know whether, for example, a low iodine concentration in the thyroid was due to rapid output of thyroxine from the gland, or to an opposite condition in which iodine was only concentrated and released slowly by this tissue. If, however, a radioactive form of iodine is given by mouth, the rate at which this particular material enters the gland can be directly determined; or when administration is discontinued, the rate with which it leaves the gland can be found (Keating and others, 1945). By this method, which appears to be of wide and general application, the dynamics of a balanced reaction within the body can be directly studied. It will be noticed that this can be done while giving only a small or normal intake of iodine during the course of the investigation. This is in contrast with the only method available hitherto, in isotope preparation which will dilute as much as will 10 micrograms of pure C^{14} and still be detectable, because it disintegrates so quickly. Instead of costing £100 it is listed in America at a few shillings. It is detectable in a different way from C^{14} because in addition to electrons it emits (like radium) X-rays of the penetrating variety called γ-rays. It is possible, therefore, to measure the activity of Na^{24} with a sheet of metal in front of the counter or—of greater biological importance—with several centimetres of tissue between the source and the counter. Three minutes after drinking some radioactive sodium chloride it is sufficient to hold a hand in front of the counter and watch the rapid absorption into the blood-stream. This element when it becomes readily available should be of the greatest interest for measurements of the extra-cellular space and of electrolyte excretion.

Another -emitter is iodine^{131} of 8-days' half-life and costing three or four times as much as sodium. It can be detected in the thyroid by tucking the counter tube under the chin. This property is not possessed exclusively by γ-emitters. Some energetic electron emitters, e.g. radio-phosphorus, can be used for the same purpose, and Low-Beer (1946) claims to be able to detect local concentrations of radio-phosphorus in a breast carcinoma by superficial exploration with the counter. In general, however, the directional sense of the counters is poor on the one hand, and on the other the body seldom localizes elements with the degree of specificity which it shows towards iodine, phosphorus and calcium. A form of histochemistry is practised with the latter elements by placing a tissue section on a photographic plate, the radio-element revealing its position by causing a blackening of the plate.

Other radio-elements of potential or actual biological application are sulphur^{35} (half-life 88 days), chlorine^{36} (greater than 1,000 years), potassium^{42} (12 hours), calcium^{45} (180 days), iron^{55} (4 years) or ^{59} (47 days), arsenic^{76} (for use in toxicology and chemotherapeutics—26 hours), bromine^{80} (4½ hours), strontium^{85} (65 days), mercury^{197} (25 hours) or ^{203} (54 days), bismuth^{210} (5 days) and some very interesting inert gases for respiratory studies, e.g. argon^{41} (110 minutes) and xenon^{127} (34 days).

I would like to conclude with a brief reference to some important biochemical discoveries made with the use of isotopes. Twenty minutes after injecting subcutaneously a solution of sodium phosphate containing radioactive phosphorus the activity of the element in the plasma reaches a peak value and thereafter falls away very rapidly as the phosphate is taken up by the tissues. By giving diminishing quantities in spread injections it is possible to maintain an approximately constant level of radioactivity per milligram inorganic phosphorus in the plasma. During this period bone and other tissues, which take their phosphorus in inorganic form directly from the plasma, will receive phosphorus of constant specific activity and if the experiment goes on long enough the whole of the bone phosphorus will ultimately have this specific activity. For example rabbit epiphyseal bone phosphorus after seven weeks has an activity 30% of the plasma phosphorus showing that 30% of the bone phosphorus has been renewed in that time. By contrast one-quarter of the phospholipid in the liver is renewed in twelve hours (Hevesy and Hahn, 1940).

If we wish to know what proportion of the phosphorus in the fæces has been absorbed in the upper intestine and re-excreted in the lower it is only necessary to compare the specific radioactivity of fæcal phosphorus with that of the plasma or even the urine. The activity in the plasma is an equilibrium value determined by the rate at which inactive phosphorus arrives from the gut and radioactive from the injections. Phosphorus returned to the bowel comes from the plasma and must have the same specific activity before dilution with unabsorbed inactive phosphorus. The method is of course equally applicable to other dietary constituents.

This kind of work throws an altogether new light on the sites of formation in the body of many substances and on the speeds at which they are formed and broken down again. It reveals that the body is a complicated chemical factory, between constituent parts of which an incessant exchange of materials is taking place. This activity could not be suspected from the relatively desultory exchanges of food and excretory-products with the environment. Only by the use of elements chemically identical with the body elements, yet distinguishable physically, has it been possible to bring this to light.

REFERENCES

Hevesy, G., and Hahn, L. (1940) *Biol. Medd. Kbh.*, 15, Nr. 7.
Low-Beer, B. V. A. (1946) *Science*, 104, 399.
Reid, A. F., and Dunning, J. R. (1946) *Physiol. Rev.*, 70, 431.

Dr. E. E. Pochin: Dr. McFarlane has given us a very clear and full account of what radioactive isotopes are, how they are produced and estimated, and what inferences may be drawn from their use in metabolic investigations. I wish now to discuss the types of problem to which they have been applied successfully. They have been used over a very wide field of work which has increased rapidly during the war, both in the United States and at Copenhagen and Stockholm. This work has hitherto concerned physiology rather more than medicine, and the illustrations which I will give are drawn commonly from this field. They show, however, how powerful and versatile is this technique of investigation, and how widely and readily it is applicable to clinical problems. I will also discuss briefly the therapeutic uses of these isotopes, although they are not strictly covered by our title, on account of the potential scope and interest of this field of experimental medicine.

We may consider first the simplest case, in which the fate of an administered chemical element is followed throughout its subsequent molecular combinations in the course of normal intermediary metabolism. It has been found, for example, that not only plants, but also animal tissues can utilize carbon dioxide in the formation of carbohydrate. For, if carbon dioxide is administered to an animal in which the carbon atom is radioactive, it is subsequently found that samples of glycogen from the body contain this radioactive carbon, and the path of its synthesis has been studied in this way through an initial condensation with pyruvic acid to oxalacetic acid and on to carbohydrate.

The same form of examination can be carried a step further by analysing the rate at which certain metabolic products are formed. For example, when radioactive iodine is added to thyroid tissue slices, the labelled iodine rapidly passes into combination as diiodotyrosine, and at the end of three hours is already present to the extent of 12% as thyroxine (Morton and Chaikoff, 1943). Similarly, iron administered by mouth has been detected in formed hæmoglobin in five hours (Pommerenke and others, 1942).

It is particularly valuable to be able to study the rates of reaction or formation of compounds, the concentration of which is ordinarily maintained in a state of stable equilibrium in the body. It has hitherto been difficult to know whether, for example, a low iodine concentration in the thyroid was due to rapid output of thyroxine from the gland, or to an opposite condition in which iodine was only concentrated and released slowly by this tissue. If, however, a radioactive form of iodine is given by mouth, the rate at which this particular material enters the gland can be directly determined; or when administration is discontinued, the rate with which it leaves the gland can be found (Keating and others, 1945). By this method, which appears to be of wide and general application, the dynamics of a balanced reaction within the body can be directly studied. It will be noticed that this can be done while giving only a small or normal intake of iodine during the course of the investigation. This is in contrast with the only method available hitherto, in which the level of the equilibrium needed to be measurably disturbed by giving a large dose of normal iodine which in itself upset the metabolism of the gland that it was designed to investigate. It has been found in a similar way that iron absorption from the gut is considerably increased, not by anæmia itself, but by depletion of the iron stores within the body. Thus in anæmia of acute onset the efficiency of iron absorption is not increased until about a week after the initial hæmorrhage (Hahn and others, 1943).

So far, we have discussed the use of tracer materials to study the course of chemical reactions and their progress in time. It is also possible by similar methods to study the rate of diffusion of materials throughout the body in just the same way as the ornithologist, who catches and rings a collection of swallows in Kent, can study the rate and route of their migration by the appearance of such "labelled" birds in different places and at different times subsequently. It is, of course, essential that the ring on the bird's leg shall not alter its powers of flight, and in exactly the same way it is essential that the radioactivity of the tracer material shall not in itself alter its metabolism or that of the tissue studied. In this way, the rates of diffusion of sodium and other materials into the cerebrospinal fluid or the aqueous humour of the eye or from the intestinal tract have been investigated, and the method is clearly applicable to a wide range of drugs or toxic materials of clinical interest. The transfer of iron to the bile in hæmolysis, or from the maternal blood-stream to the fœtus (Pommerenke and others, 1942), has been similarly investigated and studies have been made on the rate of absorption of substituted insulin molecules from the skin when given in different forms designed to delay absorption (Reiner and others, 1943).

It is a simple matter by these means to investigate the extent within the body through which various compounds or structures are free to diffuse. For example, the blood volume has been estimated, by giving a known amount of red cells labelled with either radioactive iron or phosphorus and, after allowing time for mixing, determining the concentration of such red cells in the sample removed, and therefore the volume within the body throughout which the total amount of cells given has been distributed. It is clearly a necessity of such an investigation that the labelling element, which is here used to mark the red cell, must remain permanently attached to that cell during the course of the experiment. This assumption appears to be sound for studies of blood volume. When, however, the length of survival of administered red cells was explored in this way, it was soon found that the iron from cells as they became destroyed was rapidly and fully utilized, after a lag of only a day or two, in the formation of new red cells within the recipient. It is therefore possible by this method to study only the initial stages of blood destruction since thereafter some of the radioactive iron is now attached to and labelling newly formed red cells. This type of criticism requires consideration in all investigations where an isotope is used to label a molecule or tissue structure.

Similarly, studies have been made on the space through which plasma proteins diffuse, by labelling these compounds in various ways. It is then found that a test dose of plasma proteins after administration rapidly becomes diffused through a space greater than the plasma volume itself by about fourfold (Fink and others, 1944). The distribution of sodium and other ions throughout the body has been similarly studied, and the absorption of inert gases in body tissues was closely investigated during the war. The last method has a possible application of considerable importance. If radioactive krypton is breathed in air of constant composition, the blood rapidly attains a constant content of radioactivity. If now the hand is placed under a Geiger counter, the radioactivity measurable within the hand as a whole is at first a measure of the amount of blood within the hand and only later of the amount of krypton which has diffused from the blood into the tissues. During the early stage, therefore, the total estimated activity within the hand is an index of its blood content, and the initial rate of increase of such activity gives an index of blood flow. It seems likely that this method may be of application in measuring the blood flow of a variety of tissues.

It will be noticed that we have been discussing a case in which the concentration of a radioactive isotope is measurable without withdrawing a sample from the body, and it is a particularly valuable feature of certain isotopes that their emissions are sufficiently powerful to be detected through the normal skin. This has been used in many ways, for example to determine circulation times between certain points, and in measuring the rate with which normal and pathological thyroids concentrate iodine.

A somewhat similar technique allows the distribution of certain elements within the tissues to be accurately studied by tissue slices or in histological sections. Since the emissions of many of these isotopes cause exposure of an X-ray film, if a film is placed in contact with a section or the tissue slice and is subsequently developed, the areas of blackening correspond to the areas in which the isotope is present or is concentrated. The distribution of administered calcium within rachitic bone has been explored in this way and the correspondence in thyroid tissue between the location of iodine and acinar cells can be similarly investigated. This method is well illustrated in Hamilton's review of the use of radioactive isotopes (1942).

Finally, the effect of these emissions can be used therapeutically in two ways. First, the easy production of large quantities of radioactive isotopes which is promised by the modern pile will allow cheap substitutes for radium to be produced in large quantities. It will be simple within a few years to obtain, for example, a radioactive cobalt with γ radiation rather harder than that of radium, and with β radiation rather more easily filtered. It would also be possible, owing to the hundreds of radioactive isotopes which exist, to select particular ones of emission and half-period suitable for particular problems.

Secondly, however, and of even greater interest, it will be possible in certain cases to use radioactive elements in producing selective irradiation of particular pathological tissues, while giving a greatly lower dosage of radiation to the body as a whole. Thus, if an element such as iodine is concentrated in the thyroid to a degree a hundred times greater than in the rest of the body, and if a radioactive iodine is given, of which most of the radiations penetrate only a short distance, a dosage within thyroid tissue can be obtained a hundred times greater than that in the rest of the body. In this way, a malignant thyroid carcinoma with metastases has been given a sufficient dose to cause its regression and possible cure (Seidlin, Marinelli and Oshry, 1946). This dose given to the whole body would cause death through radiation sickness. Iodine has been used in this way to produce controlled atrophy of most of the over-acting gland in thyrotoxicosis. Use has also been made of the fact that phosphorus is concentrated three times as highly in certain malignant tissues as it is in the body generally. Cases of leukæmia, multiple myeloma, and lymphosarcoma have been treated in this way, but without appreciably greater success than is obtainable with X-rays. Such opportunities for therapy may, however, develop with increasing knowledge of the concentration ratios in certain tissues and tumours of rare or hitherto unimportant metals or elements, or by the use of special devices such as the administration of radiobrominated dyes or insoluble chromic phosphate particles which are concentrated within the reticulo-endothelial system.

The whole study of concentration ratios of the lesser-known elements is likely to prove of great importance not only in therapy but in the safety of investigational methods. It is simple to calculate a dose of radioactive isotope which can safely be given to man without causing appreciably more ionizations within the body than are already caused by cosmic radiation each day, provided that it can be assumed that this material will not be selectively concentrated in some vital region. If, however, any such concentration occurs, a toxic level may be reached locally, although the average for the body as a whole is entirely harmless. While such an event appears unlikely in many instances, and has not been recognized in the many investigations made on man in the States and in Scandinavia, it is an important possibility to be excluded, particularly when a new element is being used. It should also be remembered that the effects of radiation on genes and chromosomes occur without threshold, and in proportion to the ionizations received, so that it is not possible to speak of a dose which is without biological effect, but merely of one in which this effect is comparable with those ordinarily received in daily life. With this proviso, and assuming that the radioactivity of the isotope given does not alter the metabolism of the tissues studied, it will be clear that the use of radioactive isotopes offers a very wide field in investigating biological and clinical phenomena.

REFERENCES

FINK, R. M., ENNS, T., KIMBALL, C. P., SILBERSTEIN, H. E., BALE, W. F., MADDEN, S. C., and WHIPPLE, G. H. (1944) *J. exp. Med.*, 80, 455.

HAHN, P. F., BALE, W. F., ROSS, J. F., BALFOUR, W. M., and WHIPPLE, G. H. (1943) *J. exp. Med.*, 78, 169.

HAMILTON, J. G. (1942) *Radiology*, 39, 541.

KEATING, F. R., RAWSON, R. W., PEACOCK, W., and EVANS, R. D. (1945) *Endocrinology*, 36, 137.

MORTON, M. E., and CHAIKOFF, I. L. (1943) *J. biol. Chem.*, 147, 1.

POMMERENKE, W. T., HAHN, P. F., BALE, W. F., and BALFOUR, W. M. (1942) *Amer. J. Physiol.*, 137, 164.

REINER, L., LANG, E. H., IRVINE, J. W., PEACOCK, W., and EVANS, R. D. (1943) *J. Pharmacol.*, 78, 352.

SEIDLIN, S. M., MARINELLI, L. D., and OSHRY, E. (1946) *J. Amer. med. Ass.*, 132, 838.

Professor A. St. G. Huggett: When will these tracer elements be available? How does one obtain them?

Dr. McFarlane: The Medical Research Council has set up an advisory sub-committee in connexion with this matter and requests from any source in this country for tracers for biological and medical purposes should be made to the Secretary of the Tracer Element Sub-Committee at the National Institute for Medical Research, Hampstead.

At the moment numerous people are waiting to receive radio-elements—mainly phosphorus, iodine, iron, and sodium—but only phosphorus is available. This comes in small consignments monthly from the U.S.A. and has so far proved adequate to the needs of eight to ten research projects. Because of the much larger amounts used in therapy, no radio-elements have so far been available for this purpose. It is hoped in one to two months' time to be able to obtain steady cyclotron supplies in this country and later larger quantities of most radio-elements are expected to be available.

Professor H. P. Himsworth: What arrangements have been made for the analysis of biological material after giving stable and radioactive isotopes?

Dr. McFarlane: The Medical Research Council has been allocated 50 Geiger counting outfits of recent design by the Atomic Energy Research Establishment at Harwell. Some of these have been delivered and all but a few are already allocated—to laboratories widely scattered throughout the country. Several firms are also offering counting outfits for sale. Stable tracer elements are also available, but their assay with the mass spectrometer is a much more formidable proposition. Several of these instruments are under construction in this country, although only two or three with biological estimations in view. One will soon be completed at the National Institute for Medical Research.

Section of Obstetrics and Gynæcology

President—JAMES WYATT, F.R.C.S., F.R.C.O.G.

[*November* 15, 1946]

DISCUSSION ON STRESS INCONTINENCE IN MICTURITION

Mr. Everard Williams: Stress incontinence is an acquired lesion of traumatic origin occurring in women in whom the function of micturition was previously normal. This definition will exclude cases of congenital origin, such as are met with in association with spina bifida, epispadias, and other gross congenital deformities. It will likewise exclude those due to degenerative changes which occur in later life, such as subacute degeneration of the cord, disseminated sclerosis and the like.

The absence of the prostate, the presence of the vagina and the different function of the urethra in women call for a difference in morphology from that which appertains to the male. To Kalisher we owe the first clear and accurate description of the anatomical points concerned. In 1900 he demonstrated the points of difference in the two sexes.

Apart from the general factors involved in maintaining the pelvic viscera in position, the localized supports of the bladder are concentrated around the urethro-vesical juncture. It is at this point that the vesical and vaginal fascias fuse, and fuse so intimately that they cannot be separated by dissection.

Furthermore, from the sides of the pelvis the lateral true ligaments of the bladder, anterior extensions of Mackenrodt's ligaments, and the anteriorly placed pubo-vesical ligaments, all become intricately blended at this point.

Kalisher further showed that the old description of the internal urethral sphincter was incorrect. The internal sphincter muscle consists of both circularly and longitudinally arranged muscle fibres. The circular fibres are not in the form of a completely encircling muscle, but are deficient anteriorly so that they have the arrangement of a sling which, in contraction, raises the floor of the urethra and holds it against the roof. They are arranged in two layers which embrace the longitudinal muscle fibres which are found in the floor of the urethra only. The longitudinal muscle fibres in their contraction depress the trigone and pull the floor of the urethra away from the roof. This disposition of fibres takes place at the point where the pubo-vesical ligaments find their insertion into the vesical fascia. The nerve supply of these differently arranged fibres is autonomic, parasympathetic stimulation relaxes the circular fibres and contracts the longitudinal fibres; sympathetic activity has the opposite effect. In contrast to what is found in the male the external sphincter muscle is of weak development and many of the muscle fibres do not encircle the urethra, but are lost in the vaginal walls. [Slides were shown from dissections on the cadaver illustrating these points.]

This description has been accepted by the leading continental gynæcologists, but is not found in British textbooks.

In the condition of stress incontinence descensus has taken place in the region of the bladder neck. The usual cause is a childbirth injury, or, less frequently, a gynæcological operation, such as hysterectomy.

Cases following operation are the more difficult to cure.

If the laceration of fascia includes the main mass of Mackenrodt's ligament as well as its anterior extension, there will be prolapse of the utero-vaginal canal in addition to the descensus of the bladder neck.

The physiology of micturition is less well understood than the anatomy. There are known to be five reflexes concerned in voluntary voiding; four are located in the spinal cord and the fifth is situated in the hind brain.

All research workers observe that the sphincter mechanism is exceedingly delicate and that in the experimental animal it responds to an increase in intravesical *tension*, not to intravesical *volume*. That is to say, a small volume of fluid rapidly introduced will cause the sphincter to open, whereas the bladder will tolerate a large volume, provided the fluid is very gradually introduced. In the cat, division of both pubic nerves (which carry no autonomic fibres) causes the appearance of stress incontinence. If the animal jumps, or is made to leap into the air, there is a small involuntary escape of urine accompanying the muscular action. (*See* "Central Nervous Control of Micturition", by F. J. F. Barrington, 1928, *Brain*, 51, 209.)

The establishment of the diagnosis and the methods of examination are well known. I shall mention only the necessity for complete urological and neurological investigation in all cases.

In order to assess the merits of the different operations, and to define their proper places, it is helpful to have some classification of the degree of severity of the lesion.

Stoeckel suggested a classification into four different categories, but I have adopted the simple division into mild and severe, omitting the transient cases in the puerperium which right themselves spontaneously (though they may be assisted by electrical therapy) and on which no surgeon would operate.

Mild cases are those in which a sudden great increase of abdominal pressure such as a cough, a laugh, a sneeze, brings about the incontinence.

Severe cases are those in which a slight increase of abdominal pressure, such as walking dowstairs, walking downhill, or the mere change of body posture, produces incontinence.

[A historical review of the different operations was given, but is omitted on account of the shortage of space.]

What is the feature common to all the operations employed in the alleviation of the condition? It is the raising of the trigone area of the bladder and the anchoring of it in the raised position. It is not the suture of a tear in the vesical fascia, nor of a torn sphincter muscle albeit distinguished surgeons have expressed the view that this is what their operation achieves.

There is a simple and more direct way of accomplishing this effect upon the trigone. With this object in view I devised and performed a new operation in 1942.

Author's operation.—With the patient in the Trendelenburg position and suitably anæsthetized, the abdominal wall is incised, but the peritoneum is not opened. Transversalis fascia is incised and the bladder exposed. The dissection is continued by light scalpel cuts until the bladder is well mobilized and the region of the neck freely exposed. The bladder wall and the investing fascia are now held in tissue forceps and traction is made to ascertain that the mobilization is adequate. By means of a fully curved needle and non-chromic catgut, the bladder wall, consisting of muscle and fascia, is sutured to the fibrous periosteum at the back of the pubis by four, or more, sutures placed in pairs on either side of the mid-line (*see* figs. 1, 2, 3, 4). If this has been correctly carried out, it will be seen on examination at a later date that the vestibule has retracted within the tissues of the vulva as is normally the case and the pathological laxity in this region has disappeared.

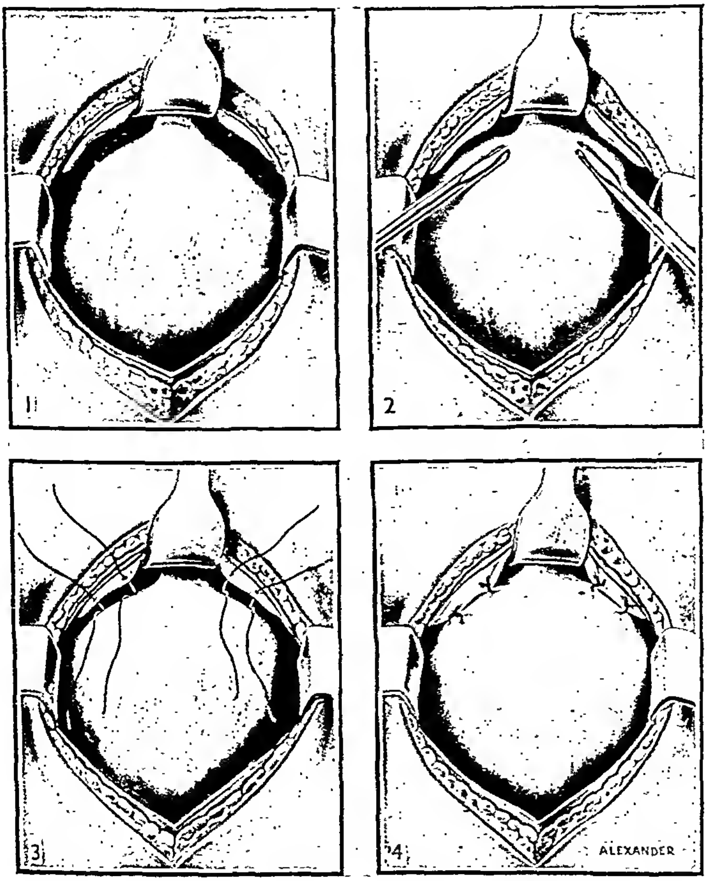


Fig. 1.—Exposure. Fig. 2.—Mobilization.
Fig. 3.—Suture. Fig. 4.—Restitution.

The bladder is not opened and the abdominal wall is closed in the usual way. A self-retaining catheter is employed for five days, and the bladder kept empty. The operation is followed by a period of difficult micturition and mild bladder irritability, but the bladder function quickly returns to normal.

The table shows the nine cases in which the operation has been performed by me since 1942. The interval 1943—1945 is explained by my absence on war service.

SEVERE CASES

No.	Name	Age	Date of operation	Last report	Comments
1	G. B.	55	Sept. 1942	2.11.46	Still perfect. 4-year cure
2	——		Cannot be traced		——
3	M. S.	40	28.8.45	18.3.46	3 para.; last 8 years ago. Forceps. S.I. since
4	H. N.	39	28.8.45	1.3.46	20 years S.I. following 1 confinement
5	M. M.	24	—.2.46	—.10.46	Extended breech "some years ago." Perfect result—4 mo. gravid.
6	E. H.	43	20.3.46	6.11.46	S.I. since birth of 2nd child 8 years ago. Asthma and ch. bron. Marion operation failed.
7	M. F.	40	—.5.46	—.10.46	1 para. 16 years ago extended breech. Fractured humerus and brachial palsy
8	E. M.	37	21.5.46	—	11 years S.I. following 1 confinement. Forceps delivery.
9	H. B.	40	—.8.46	—.10.46	Cured so far. Forceps delivery 20 years. ago. S.I. since confinement

There is one four-year cure and one case (No. 11) in which there was recurrence after eight months. The latter was a subject of severe asthma and chronic bronchitis, and during these eight months a mild degree of utero-vaginal prolapse had become accentuated.

POSTSCRIPT.—(i) A Fothergill repair has since been performed on this patient.

(ii) Case 5 (M. M.) has recently been delivered of a healthy baby; she remains cured.

Mr. Terence Millin: There are four main types of stress incontinence: (1) Congenital sphincteric weakness. (2) Post-puerperal, which will frequently go on to spontaneous recovery, and often benefited by faradic stimulation. (3) Menopausal, which may respond to hormone therapy. (4) The commonly met with stress or orthostatic incontinence, usually coming on some years after childbirth, and commonly associated with vaginal laxity.

My interest in the subject dates back more than ten years, when I first met a group of young girls suffering from a congenital form of urinary incontinence not due to any apparent neuropathy. For obvious reasons vaginal intervention was to be avoided, and I searched the relevant surgical literature without getting much help. Cysto-urethroscopic investigation of these cases revealed in all a patulous bladder neck, and I evolved and practised the intravesical tautening operation, which I described to the Section of Urology in January 1939 (*Proc. R. Soc. Med.*, **32**, 777). This entailed a generous excision of the posterior lip of the bladder neck, with a wedge running into the upper urethra. The cut edges of urethra and bladder neck were then approximated snugly around a No. 4 catheter, which was then removed, and suprapubic drainage maintained for ten days.

The results in these congenital cases were so gratifying that when confronted with a multipara who had undergone three vaginal interventions without cure of her stress incontinence, I applied this intravesical operation combined with a Goebell sling of ribbon catgut with complete cure. I operated upon more than a score of such cases by this technique with satisfactory results on the whole. Here is an illustrative case: Mrs. C., aged 38, still suffering from marked stress incontinence, almost complete, despite a colporrhaphy. Intravesical operation with immediate complete cure. Two years post-operatively she developed a severe attack of whooping-cough, and, despite this, there was no incontinence. Now five years post-operatively she remains a complete cure.

Despite such results, I felt that it should not be necessary to open the bladder in the acquired type of case, as there was seldom any apparent intrinsic bladder-neck deficiency, and the intervention was followed sometimes by a troublesome basal cystitis. I lacked the courage at first to abandon the intravesical tautening, but shortened the period of suprapubic drainage, and added a fixation of the bladder neck to the tendons of the recti close to the pubis in an attempt to draw up and fix the ptotic structure. This differed from the ventrofixation of the bladder employed many years ago by Victor Bonney in selected cases. His operation had the demerit of fixing the elastic anterior bladder wall which stretches so that this operation does not give lasting results. This idea of fixing the bladder neck to the back of the pubis has recently been revived by Perrin of Lyon, and has been termed cervico-cystopexy. I feel that there is always the risk of perforating the mucosa, and of the thread or silk becoming a nidus for phosphatic deposits.

Convinced that the essential requirement for cure was elevation of the bladder neck I devised my "muscle hammock" or "sling" operation, which I have now used for more than two and a half years with great satisfaction. The Goebell operation and its various modifications, notably those of Stoeckel and Frankenheim, did not appeal owing to the difficulty of assessing the exact degree of tension required in the sling, as one end was attached to a fixed bony point, namely the pubis, the free end being fastened to the aponeurosia. Undue tension would lead to dysuria, or even retention, and insufficient tension to a complete or partial failure. My idea was to elevate and suspend the bladder neck by a sling supported at each end to muscle, so allowing for a variability of tension. By relaxing the abdominal wall as in the normal position adopted for micturition, the sling would be relaxed, and on tightening the abdominal wall, as inevitably occurs when the intra-abdominal pressure rises as in coughing, sneezing, running, &c.—the precise factors causing a stress incontinence—the sling is actually tightened, and the bladder neck drawn upwards.

Before giving the details of this operation I shall briefly review the other procedures in use. They may be grouped roughly thus:

(1) The vaginal operations of Kelly, Bonney, Marion, &c., which aim at elevating the bladder neck by buttressing this structure from below by gathering in the stretched or torn subjacent fasciæ. The Kelly school believe that the sphincter must be reefed at the same time, but my cysto-urethroscopic studies and experience with the intravesical operations for the condition showed no intrinsic sphincteric laxity. I cannot confirm the findings of Macky, who claimed to show the torn ends of the sphincter intravesically and to suture them. Kennedy of New York, who has given much thought to the problem (describing incidentally various urethral sphincters), believes that it is necessary to free extensively the bladder neck and urethra from the back of the pubis. He then plicates the urethra and approximates the fasciæ. His procedure is supported by Counsellor of the Mayo Clinic. Others, however, maintain that this operation is unnecessarily heroic, and stress that very troublesome bleeding can occur, necessitating packing. Be that as it may, Kennedy's concept of the underlying pathology—namely a bladder neck that is dropped and, as he thinks, fixed in its false position—is similar to mine.

(2) The second group of operations are those which rely on narrowing the urethra. Into this group fall the rotations of the urethra, which I feel, in common with most workers, should be condemned whole-heartedly. Lowsley of New York frees the urethra on its anterior aspect, and plicates the bulbo-cavernosi muscles with ribbon catgut. The anatomo-pathology underlying this procedure is difficult to see. Others, following Giordano, use gracilis or part of it, to lap the urethra, but such operations also fail to recognize the essential pathology underlying the condition.

SEVERE CASES

No.	Name	Age	Date of operation	Last report	Comments
1	G. B.	55	Sept. 1942	2.11.46	Still perfect. 4-year cure
2	———		Cannot be traced		———
3	M. S.	40	28.8.45	18.3.46	3 para.; last 8 years ago. Forceps. S.I. since
4	H. N.	39	28.8.45	1.3.46	20 years S.I. following 1 confinement
5	M. M.	24	—.2.46	—.10.46	Extended breech "some years ago." Perfect result—4 mo. gravid.
6	E. H.	43	20.3.46	6.11.46	S.I. since birth of 2nd child 8 years ago. Asthma and ch. bron. Marion operation failed.
7	M. F.	40	—.5.46	—.10.46	1 para. 16 years ago extended breech. Fractured humerus and brachial palsy
8	E. M.	37	21.5.46	—	11 years S.I. following 1 confinement. Forceps delivery.
9	H. B.	40	—.8.46	—.10.46	Cured so far. Forceps delivery 20 years ago. S.I. since confinement

There is one four-year cure and one case (No. 11) in which there was recurrence after eight months. The latter was a subject of severe asthma and chronic bronchitis, and during these eight months a mild degree of utero-vaginal prolapse had become accentuated.

POSTSCRIPT.—(i) A Fothergill repair has since been performed on this patient. (ii) Case 5 (M. M.) has recently been delivered of a healthy baby; she remains cured.

Mr. Terence Millin: There are four main types of stress incontinence: (1) Congenital sphincteric weakness. (2) Post-puerperal, which will frequently go on to spontaneous recovery, and often benefited by faradic stimulation. (3) Menopausal, which may respond to hormone therapy. (4) The commonly met with stress or orthostatic incontinence, usually coming on some years after childbirth, and commonly associated with vaginal laxity.

My interest in the subject dates back more than ten years, when I first met a group of young girls suffering from a congenital form of urinary incontinence not due to any apparent neuropathy. For obvious reasons vaginal intervention was to be avoided, and I searched the relevant surgical literature without getting much help. Cysto-urethroscopic investigation of these cases revealed in all a patulous bladder neck, and I evolved and practised the intravesical tautening operation, which I described to the Section of Urology in January 1939 (*Proc. R. Soc. Med.*, **32**, 777). This entailed a generous excision of the posterior lip of the bladder neck, with a wedge running into the upper urethra. The cut edges of urethra and bladder neck were then approximated snugly around a No. 4 catheter, which was then removed, and suprapubic drainage maintained for ten days.

The results in these congenital cases were so gratifying that when confronted with a multipara who had undergone three vaginal interventions without cure of her stress incontinence, I applied this intravesical operation combined with a Goebell sling of ribbon catgut with complete cure. I operated upon more than a score of such cases by this technique with satisfactory results on the whole. Here is an illustrative case: Mrs. C., aged 38, still suffering from marked stress incontinence, almost complete, despite a colporrhaphy. Intravesical operation with immediate complete cure. Two years post-operatively she developed a severe attack of whooping-cough, and, despite this, there was no incontinence. Now five years post-operatively she remains a complete cure.

a very weak abdominal wall following several laparotomies. I hesitated to advise a sling, but was rather pushed into it. During the operation the catheter escaped from the urethra, and I asked an attendant nurse to reintroduce it. The slings were duly passed round the tube containing the catheter, but at the end of the operation it was found that the catheter was no longer in the bladder but in the vagina. As bad luck would have it the vagina was grossly infected, with the result that infection travelled along the slings which had penetrated the vagina and presumably sloughed. She left hospital as bad as ever. Six months later I heard from her doctor that she was completely cured. Presumably the fibrosis had fixed the bladder neck in the elevated position. It is interesting to note in this connexion that Studdiford has reported that the best results after the Aldridge procedure are noted only nine months later. The reason is not apparent. With my sling I have not found this, and expect an immediate cure of the incontinence.

Operative difficulties.—These are two in number: First, bleeding. From time to time the deep dorsal vein of the clitoris is torn in freeing the upper urethra, and troublesome bleeding can occur. This is best taken care of by means of the coagulating current. I have experienced it only rarely. Secondly, the difficulty in freeing the urethra from the underlying vagina. If too forcible or meticulous freeing is indulged in, the urethra or bladder may be torn, thus leading to suprapubic leakage after the catheter is withdrawn. This will necessitate the reintroduction of the catheter. Since employing the special forceps for tunnelling this accident has not occurred.

Post-operative difficulties.—(*a*) *Urinary leakage*: This I have already mentioned.

(*b*) *Retention* on withdrawal of the catheter. If the patient has not passed urine four hours after removal of the catheter it should be reintroduced. In two cases in which the bladder was allowed to become unduly distended the abdominal wall was on guard, the slings correspondingly tightened, and catheterization was exceedingly difficult, and, in one case, impossible, necessitating a temporary cystostomy. Should this contingency occur it would appear preferable to puncture the bladder by needle suprapubically to relax the structures and then reintroduce the catheter *per urethram*.

(*c*) *Late urinary difficulty*: Two cases have been seen with this complaint, which rapidly responded to a dilatation of the bladder neck.

(*d*) *Basal cystitis*: From time to time a urinary infection will follow as may always occur where urethral instrumentation is necessary, and prove troublesome. Sulphanilamides are administered routinely during the five days the catheter is in situ as a prophylactic.

To sum up, I feel that the congenital type of case, excluding neuropathies, should be treated by intravesical sphincteric tautening along the lines I laid down in 1939. In the acquired cases, and these constitute the vast majority, a properly conducted colporrhaphy and urethroplasty will secure a high proportion of successes. There remains, however, a not insignificant group, where either vaginal intervention by a competent operator has failed, or where no cystocele or urethrocele exists. In these I put in a plea for my sling procedure, which I feel is based on sounder principles than any other yet devised. The psychological trauma of repeated failed vaginal interventions for this distressing form of urinary leakage is immense, and there are few more grateful patients than those cured by a sling after 3, 4, or 5 failed colporrhaphies.

Professor J. Chassar Moir: In May 1944, at a combined meeting of the Sections of Urology and of Obstetrics and Gynæcology, the subject of bladder dysfunction following childbirth was discussed (*Proc. R. Soc. Med.*, 38, 653). I then had the privilege of presenting the case for the "fascial-sling" operation, and of showing a

(3) The third group comprises the suspension operations from above. Mechanically it is always sounder to pull than to push. The Goebell procedure was the prototype, and I have given my reasons for not liking this operation. Many have found it difficult to isolate the bladder neck by the superior approach, and some, like Michon in Paris, use a combined approach, i.e. free the bladder neck from below and then pass the Goebell sling from above. This I have found neither necessary nor desirable. The Aldridge technique is another combined operation now popular, but takes over an hour to perform with all the disadvantages of change in position of the patient, double set of instruments, and change of gown and gloves. I dislike the passing of forceps from the vagina into the retropubic fatty spaces. The modifications of the Goebell operation by Thompson and Miller, wherein the slings are passed anterior to the pubis, merely elevate the lower urethra and so are unsound.

The sling operation I have devised may be thus briefly described:—An 18 Ch. self-retaining catheter is introduced, the bladder emptied and catheter drawn down so that the expanded head is in close proximity to the bladder neck. The vagina is then lightly packed. Transverse abdominal incision, three fingerbreadths above the pubis, is deepened through the skin and subcutaneous tissues, the flaps being undermined. The aponeurosis is now incised in the line of the skin incision, and two straps, each one centimetre wide, are cut from the lower aponeurotic leaf. It should be noted that the pedicles in these straps are muscular. The recti are now separated in the mid-line, and the retropubic space opened up by means of a self-retaining retractor. The bladder neck and urethra are readily identified, thanks to the indwelling catheter. My specially devised curved forceps is then passed below the urethra. Opening the blades enlarges this sub-urethral tunnel, and permits the passage of the aponeurotic straps after being threaded through the outer borders of the recti. The straps are drawn taut and sutured to each other by means of nylon. The space is dusted with sulphanilamide powder, and drained by means of corrugated rubber introduced through a stab incision immediately above the pubis. Aponeurosis and skin are closed. The catheter is retained for five days.

In what type of case do I advocate this operation? Not in every case of stress incontinence, to be sure, for those associated with a definite cystocele or combined cystocele and rectocele, should certainly be operated upon from below, and cure will be obtained in 50% to 80% of cases according to the skill of the operator. Though this may occasion some surprise, these are published figures and correspond with what my own researches have shown. Many apparent cures seem to relapse twelve to eighteen months later due to stretching of the sutured fasciæ. The fact that so many different operations have been designed to remedy the condition shows that the vaginal interventions fall short of a 100% cure ratio. Where a properly conducted vaginal repair has failed to cure the incontinence then I believe that my sling procedure should be employed. In the group of cases where no cystocele is present, and in the nulliparous, I advise a sling in the first instance. Bonney's test of supporting the bladder neck on either side with a finger *per vaginam* and requesting the patient to cough demonstrating that loss of urine will not occur under these conditions, supports my contention that all that is required to cure the condition is permanent elevation of the bladder neck, and that plication of the sphincter or urethra is quite unnecessary.

Results.—I have now performed the operation 67 times. I have records of only one case which relapsed. This woman had had two previous colporrhaphies and a failed intravesical tautening. She left the hospital apparently cured, but when seen five months later was again incontinent. There is one particularly interesting case who had a severe degree of incontinence following a colporrhaphy. She had

We must now decide which method is easiest, safest and surest. In my opinion, the Aldridge operation is easiest, and it also avoids a disadvantage inherent in both the Studdiford and Millin operations of a wide opening up of the space of Retzius. In the Millin operation, there also seems to be a distinct hazard of penetrating into the vagina, or of damaging the urethra or neck of the bladder in passing the dissecting instrument down from above. On the other hand, it avoids the complication of a combined abdominal and vaginal dissection. The risk of infection (never very great) is also presumably lessened.

In the technique of the Aldridge operation the only step in the dissection presenting difficulty is the starting of the "tunnels". The colporrhaphy dissection should be carried slightly further than usual to the sides of the upper urethra. The operator then locates the descending ramus of the pubis with his finger, and by a little sharp dissection gains access to the structures at the inner margin of that bone, an inch, or a little more, below and lateral to the under-margin of the symphyseal joint. At that point, a firm layer of fibrous tissue will be felt preventing access to the space of Retzius. With blunt-pointed, curved scissors, firm pressure is put on the tissues at the edge of the bone (avoiding periosteum), and by making a few snips a passage is broken open which can then be enlarged with the point of the finger. It is now an easy matter to pass the finger up behind the pubic bone to meet the abdominal dissection.

A second difficulty is to judge the correct tension to put on the fascial strips when they are united. I draw the strips down fairly firmly and make them cross under the urethra. At this point a fine nylon suture is inserted. A catheter is now introduced into the urethra; if it can be pushed into the bladder fairly easily, but at the same time can be felt to negotiate a decided "bump" or "ridge" at the level of the sling, all is well, and two or three further nylon stitches are then inserted to secure the fascial strips. If, however, matters are not as described, the first nylon stitch is removed and the necessary adjustments made. Finally, instead of cutting off the redundant ends of the strips, they are made to cross over, and are anchored by further sutures to the tissues at the sides of the bladder.

Catheter drainage is maintained for ten days during which time the patient is given sulphanilamide, 0·5 gramme, four-hourly. The catheter should be inserted so that its "eye" is 3 in. distant from the external urethral meatus, and it should be anchored by a firm stitch to the tissues of the anterior lip of the urethral meatus.

Finally, I should like to refer to the use of the sling operation in patients who have had a vesico-vaginal fistula repaired, but who, because of extensive destruction of the sphincteric region of the bladder, are still incontinent of urine. In a series of some 36 cases of vesico-vaginal fistula successfully closed by vaginal operation, I have had 7 in which a seemingly perfect result has been marred by a slight or severe degree of urinary incontinence. (2 of these were cases in which the entire urethra had been destroyed, and in whom a new urethra had been fashioned by the Gray Ward technique.) By use of the fascial sling, 2 patients have been completely cured, and 2 others have been very greatly relieved. In one further case (a urethral reconstruction) the operation was unnecessary for great relief was obtained by use of a Hodge pessary, inserted in such a way that the rounded end pressed forward on the urethra. This patient learned to insert the ring herself each morning; and from being completely "house-bound", she has become able to earn her living as a secretary and has recently re-married. The two remaining patients are still awaiting treatment by the sling operation.

REFERENCES

ALDRIDGE, A. H. (1942) *Amer. J. Obstet. Gynec*, 44, 398.
STUDDIFORD, W. E. (1944) *Amer. J. Obstet. Gynec.*, 47, 764.

patient who had been successfully treated by this method for stress incontinence of urine that had persisted after the closure of an extensive vesico-vaginal fistula.

In my opinion the fascial sling operation should be strictly reserved for the case in which the simpler and safer procedure of colporrhaphy, together with a tightening of the tissues below the bladder neck, has been tried and has been found unsuccessful. It has been stated to-night that the failures following the orthodox colporrhaphy amount to not less than 40% of cases. This is contrary to the experience of most gynæcologists (*see* Stallorthy, J., *J. Obstet. Gynæc.*, 1940, **47**, 391), and I cannot allow so pessimistic a statement to pass unchallenged. If the operation is adequately performed the failure rate should be very much less, although I agree that it is far from negligible.

In 1929 I saw Werner of Vienna perform the Goebell-Stoeckel operation. Two narrow ribbons of fascia were dissected down from the anterior abdominal wall and left attached to the pyramidalis muscles. With the patient in the lithotomy position, exposure of the urethra and bladder neck was then made as in the orthodox colporrhaphy operation, and a tunnel opened up into the space of Retzius on both sides. The fascial bands were now pulled down by means of long forceps and were united under the neck of the bladder.

In 1942, Aldridge described a modified technique in which strips of fascia were dissected from the abdominal wall, above, and parallel to, the inguinal ligaments. These strips were left attached to the recti muscles about one inch above the pubis. The remainder of the operation was as already described, save that the vaginal repair included an infolding and tightening of bladder fascia as is usual in a colporrhaphy.

Later, Studdiford advocated another modification. After making the tunnels at the sides of the upper urethra, he completed the colporrhaphy and closed the vaginal incision. He then dissected down a single, long, vertical strip of fascia from the front of the recti muscles leaving the base attached about 1 in. above the pubis. This strip was then mounted on an aneurysm needle and pushed down through one of the previously dissected tunnels, round the upper urethra, then up through the other tunnel, to be attached to the fascia of the opposite rectus muscle. Thus, a single sling of fascia extended from the lower end of one rectus muscle to the lower end of the other. This technique differed from that of the Goebell-Stoeckel operation in eliminating the need for joining two fascial strips under the urethra.

My assistants, Mr. Scott Russell and Mr. G. G. Lennon, and myself have tried both the Aldridge and Studdiford techniques with success. The first operation has the merit of simplicity and is, on the whole, the one I favour. The second requires a wide separation of the recti muscles and a considerable pushing down of the bladder from the inner side of the symphysis pubis (i.e. opening up the space of Retzius) in order to give sufficient access to the upper urethra. And there are other disadvantages. In dissecting up the fascial strip a good deal of trouble is experienced from numerous bleeding points; and when the strip is finally obtained, it will be found that there are weak spots corresponding to the tendinous intersections which are liable to tear if more than a moderate pull is exerted.

It may be worth mentioning that in one of my cases there had been so many previous abdominal operations that it was impossible to find a clear space on the abdominal wall from which to dissect up a fascial strip. I therefore obtained a fascial strip from the thigh and inserted it to form a sling after the manner of the Studdiford operation. An excellent result was obtained.

I have not had any experience of the new and very successful Millin operation, but it seems to me that the various sling operations all achieve the same end-result.

We know that a badly conducted third stage of labour can cause post-partum hæmorrhage, the bad conduct consisting usually of feeble attempts to express the placenta by massaging it and pushing the uterus downwards. This downward pressure of the uterus I consider a dangerous thing; possibly it causes uterine engorgement by hindering the flow of blood in the uterine veins, and if the uterus is to be touched at all, I consider it should be held with a wide grip suprapubically, and, if anything, pushed upwards rather than downwards.

Supposing that hæmorrhage now occurs, attempts at Credé's expression are made, but fail. There is no advice we can give the midwife except the manual removal of the placenta, which, in a primigravida, I doubt if a midwife could do on her own, the patient being given no anæsthetic. Even if the midwife could perform this operation, it would be extremely dangerous by causing shock in the already exsanguinated patient.

Under these circumstances the midwife is discouraged from using any oxytocic drug, chiefly on account of the danger of the formation of a constricting ring. If this danger were not present, the drug might well make the attempted manual removal unnecessary.

About 1935, in the Obstetric Unit of University College Hospital, thanks to Professor F. J. Browne, 0·5 mg. ergometrine was given intramuscularly to 500 consecutive normal cases, as soon as the head was delivered. In no case was there any evidence of a constricting ring, and in no case was manual removal necessary, nor was there any other catastrophe such as acute inversion of the uterus. Mr. Peel tells me that a similar experiment has been carried out at King's College Hospital, using 5 units of pituitary extract. In this much smaller series of cases, I believe about 100, a constricting ring occurred twice. It would seem therefore that this danger is very real with the use of pituitary, but I have yet to see cases or hear of this occurrence attributable to ergometrine.

I am not suggesting that we should teach the routine use of ergometrine during the third stage. Personally, in cases of third stage hæmorrhage I have no hesitation in giving 0·25 mg. intravenously, but I do suggest that we should advise the intramuscular injection of ergometrine before manual removal is attempted. Having removed the placenta, it is universally agreed that oxytocic drugs may be used, and at this point I would like publicly to deprecate the impertinence of some local supervising authorities who forbid their midwives to carry any oxytocic drugs.

By this action they remove a powerful weapon from the midwife's armament, placing the life of every patient in their area in unnecessary and unjustifiable danger. Which of us would like to attend a confinement without having some oxytocic drug available?

The placenta removed, severe bleeding is now best controlled by bi-manual compression. Again, a difficult and somewhat dangerous procedure in the unanæsthetized patient. How many of you have tried this manœuvre with both hands on the abdomen?

A broad suprapubic grip on the uterus is maintained and the other hand placed on the posterior wall of the uterus *per abdomen*. Unless the patient be grossly fat, it is surprising to find how efficiently the placental sinuses can be compressed by this method.

Professor Hilda N. Lloyd: *General remarks.*—Management of the third stage of labour in normal cases is the management of the whole labour—the first and second stages having managed themselves. It is the one stage where interference and meddlesome midwifery can do more harm than at any other time. It is important to know and to teach students and nurses what is happening during the third stage of labour.

Mr. D. M. Stern said that he thought the attitude to the treatment of stress incontinence was too symptomatic.

There was more than one cause for this condition, and only a careful study of each patient, and a knowledge of a normal physiology and anatomy of micturition would enable one to make an accurate diagnosis before attempting a cure. This was confirmed by the varied success met with in the different operative procedures.

The causes can be grouped under five headings: (1) Cystocele. (2) Prolapse of the urethra. (3) Damage to the internal sphincter. (4) Rupture of Bell's muscle. (5) Extrapelvic causes, such as spina bifida and neurological lesions.

In a series of 77 cases, 60 were due to cystocele with, or without, urethral prolapse, 11 to urethral prolapse only, 2 to rupture of Bell's muscle, 2 to damage to the internal sphincter, and 2 to extrapelvic causes.

Fixation of the urethra by the vaginal approach cured those cases due to urethral prolapse. There are only two failures in the whole series, and both of these were complicated by fistula with extensive loss of tissue, due to trauma and infection.

[*January* 17, 1947]

DISCUSSION ON THE MANAGEMENT OF THE NORMAL THIRD STAGE OF LABOUR AND OF HÆMORRHAGE THEREIN

Mr. J. D. S. Flew: In the majority of textbooks the advice given concerning the third stage is stereotyped. The patient is turned on to her back, a hand is placed on the abdomen, signs of placental separation must then be awaited, after which the placenta is expressed and then, if necessary, oxytocic drugs may be given. Should excessive bleeding occur, the placenta must be removed either by Credé's method or by manual removal, after which the bleeding is controlled by oxytocic drugs, possibly a hot intra-uterine douche, and—if these methods fail—bi-manual compression.

Little or no research has recently been published on the mechanics of the third stage of labour. It is believed that placental separation is initiated by uterine retraction, but this alone is insufficient.

Barbour in 1899 showed that the placental site could be diminished from approximately 38 sq. in. down to 14 sq. in., as a result of which no placental separation occurred. This was demonstrated in the case of a uterus removed by Porro's operation, and no retroplacental hæmatoma was present.

This is the second factor which normally causes placental separation, the third being the pressure of the uterine walls bearing down on the placenta.

It is customary to teach that the signs of placental separation are the rising of the fundus, the gush of blood *per vaginam*, and the permanent lengthening of the cord. These of course are signs of placental descent rather than actual separation, the separation having occurred beforehand.

If uterine retraction initiates placental separation, then surely this will commence at the time of maximum retraction, namely at the moment of the birth of the child's body, and we then wait for the secondary factors to complete the process.

I am not so much concerned as to how you and I conduct the third stage of labour, or deal with cases of excessive hæmorrhage; doubtless we express the placenta at once, and possibly at times aid this process by traction on the cord. Rather I am concerned here with what we teach our students and, in particular, our pupil midwives, on how to conduct the third stage of labour and the management of excessive hæmorrhage. Once qualified, the midwives conduct 60% of the midwifery of this country without a medical practitioner being present, and I doubt if the routine advice given to them is the best for the patient.

In those cases requiring methedrine this response usually takes place and is almost always permanent.

Fluid (water) by mouth is encouraged.

The patient is then anæsthetized with pentothal after full cleansing and catheterization. Usual amount required 0·25 gramme. If placenta still in uterus (most cases) manual removal carried out without any attempt at expression.

Amyl nitrate given for cases with contraction ring—not always effective when severe probably because of light anæsthesia.

Ergometrine 0·125 mg. given i.v. as placenta is removed. (Hot douche is rarely necessary in these cases and usually no further hæmorrhage is encountered.) This is chiefly due to the lightness of the anæsthesia.

Perineum examined and perineorrhaphy performed if required.

Blood.—Total amount given: In some cases 2 pints at least sometimes 3 pints. All Group 0 Rh negative. No cross matching performed. The blood testing is reliable and this is not necessary.

Follow-up. On fifth day full blood-count carried out by Blood Transfusion Service. If hæmoglobin is below 50% (rarely) then further blood transfusion is given. (Plasma not given if avoidable now in view of risk of homologous serum jaundice.)

Dr. Peter Denham, *Assistant Master, Rotunda Hospital, Dublin*: Fundal control during the third stage, practised in the Rotunda from 1786 and before, and known as the Dublin method, has been abandoned at the Rotunda for almost twenty years. The normal third stage is now conducted without any such control.

Routine of normal third stage, after spontaneous delivery, uncomplicated breech or low forceps, not involving any long or deep anæsthesia and after a labour not unduly prolonged: The patient is delivered in the left lateral position or turned back into it after delivery and remains in that position during the third stage. Her condition is noted now and observed all through by the labour ward Sister. After the cord has been divided and dressed the student midwife returns to the couch to observe the patient's condition and ready to swab down the vulva and perineum using a sponge holder. When the cord lengthens and a gush of blood indicates the separation and expulsion of the placenta into the vagina the Sister may feel the fundus and note the other signs of separation and expulsion. Then a catheter is passed and the uterus is rubbed up and gentle and intermittent pressure on the fundus expels the placenta and membranes intact from the vagina. After this the uterus is rubbed up every five minutes for the next half-hour and at frequent intervals for the next three hours.

This routine is modified in certain cases: (1) History of previous post-partum hæmorrhage. (2) Operative deliveries that may be associated with damage. (3) After prolonged labours and deep anæsthesia. (4) Cases of ante-partum hæmorrhage.

(1) *Prophylaxis* for those patients who have had a P.P.H. on a previous pregnancy: They are given extra calcium, in the form of osteocalcium two tablets t.i.d., vitamin K one tablet b.d., for the last three weeks of pregnancy. They are admitted at 38 weeks and given 2½ grains of quinine daily. That is all, until at delivery we administer 5 units of pituitrin when the head is crowned, and control the fundus in order to be ready for manual removal.

(2) After a difficult and traumatizing delivery, e.g. craniotomy or difficult version, we do not hesitate to perform an immediate manual removal to secure these advantages: (*a*) Rupture may be diagnosed or excluded, e.g. after a difficult internal version. (*b*) We are then in a strong position in regard to the administration of oxytocics. (*c*) The placenta is not going to come down over an incompletely

repaired perineum. (*d*) Later interference will not be necessary, and no second anæsthetic will be required.

(3) Similarly, after a very long labour, e.g. inertia, immediate manual removal is indicated.

(4) The danger of this period to cases of ante-partum hæmorrhage is hardly sufficiently stressed. The accidental hæmorrhage usually presents no difficulty, the placenta coming away immediately but even the minimum of loss may be enough to turn the scales. The danger in cases of placenta prævia is greatly increased as, the placental site being in the non-retractive part of the uterus, there is not the same control of P.P.H. These cases must be given oxytocics and the fundus well and continuously controlled if disaster is to be avoided. I would like to mention that over the last twenty years almost one-half of those who died of placenta prævia died of P.P.H.

The *abnormalities* that arise at this period are chiefly four: (1) Hæmorrhage before delivery of the placenta. (2) Hæmorrhage after delivery of the placenta. (3) Retention of the placenta without hæmorrhage. (4) Obstetric shock.

I am deliberately excluding cases of traumatic P.P.H., as they are only due to lack of skill on the part of the attendant, also cases delivered abdominally are in a category of their own.

(1) If hæmorrhage is noted without the signs of placental separation we pass a catheter, rub up the fundus, and make an effort to express the placenta by Credé's method gently. If this fails the patient is anæsthetized and the manœuvre is again attempted once. Manual removal is then resorted to without further delay.

We feel strongly that if Credé's method is persisted in it may become a brutal and shocking procedure and that with chemotherapy at even its present level manual removal is not an operation to be feared.

The technique of manual removal needs no description except to say that the hand is always introduced a second time to make sure that no cotyledon has been left behind; and to perform a bi-manual massage. Oxytocics are now given. The uterus always responds to this routine but if it did not plugging would now be resorted to. (This has only been done once in the three years in a case of placenta prævia. In another case, a woman was brought in moribund from hæmorrhage, the placenta had already been delivered and she died ten minutes after admission while being plugged.)

(2) After delivery of the placenta we have always been able to control any hæmorrhage by rubbing up the uterus abdominally and administering oxytocics, except in one case who had a rupture of the vaginal vault and uterus during a spontaneous delivery.

(3) Retention of the placenta. In the absence of hæmorrhage we leave the uterus alone for half an hour, unless there is indication that the placenta has separated or that something is wrong. At the end of that time a catheter is passed, a hand is placed on the abdomen. This often reveals that the placenta is lying in the vagina (where it may well have been for the past twenty minutes if the attendant has not been observant). During this time the operator is quietly observed by Sister to make sure that he is not yielding to temptation and becoming *fundus fiddler*.

If the placenta is still *in utero* no cause for alarm is felt. The trolley is prepared for a manual removal and a further period of half an hour is allowed to elapse during which the fundus may be palpated twice, as before, to see that the placenta has not come away in the meantime and that the uterus has not filled up with blood. . . . At the end of this time an attack may be made on the patient by Credé's method. I deliberately say "attack"; this shocking manœuvre often only partly separates the placenta and causes bleeding to start. It is never to be attempted without adequate resuscitation measures being ready and waiting. If the first effort is not crowned with success we may try again under anæthesia and then go on to manual removal. Thus we take half an hour to be the normal duration of the third stage, but do not consider anything less than an hour to warrant interference, in the absence of hæmorrhage. The injection of saline along the cord is occasionally done, but it only acts in my opinion by giving Nature a little more time to act, and it is only used as a demonstration for teaching purposes. In the presence of hæmorrhage it is an unjustified waste of time.

(4) Obstetric shock, that is to say unexpected shock coming on an hour or so more after the completion of the third stage, is a condition I have not met. I have seen patients collapse and even die two hours after delivery, particularly bad cases of toxæmic accidental hæmorrhage who responded well to the earlier treatment at the time of delivery, and appeared out of danger only to collapse in this way some two hours later. I have always considered this to be due to neglect on my part in that the restorative measures have been abandoned too early and this secondary shock (Moon) had developed. Also absorption of toxæmic elements from the apoplexy in the uterine muscle has probably a bearing on the causation. The cases reported from time to time are usually due to unrecognized loss, possibly in a patient already anæmic. That there is a special type of shock unassociated with trauma or hæmorrhage made for the scourge solely of obstetricians I am very loath to believe.

The results achieved are as follows:

Vaginal deliveries	*Manual removal*	%	
7,284	69	0·95	Rotunda
6,086	77	1·2	Glasgow
2,685	43	1·6	Edinburgh

Stander in William's "Obstetrics" claims 0·2% but the report of the New York Lying-in Hospital (1939) shows almost three times this with an incidence of inversion of the uterus of 1/4,000, a condition that has not been seen in the Rotunda for at least twenty years.

Mr. G. F. Gibberd: In the management of the third stage of labour, three issues only were discussed, because they were probably the most debatable. Reasons were given for taking the following views: (*a*) That throughout the third stage of labour the hand should "guard" the fundus of the uterus more or less continuously; (*b*) that oxytocic drugs should never, in any circumstances, be given before the delivery of the placenta; (*c*) that, provided that the patient is in suitable surroundings, delay of two hours in the third stage of labour is a proper indication for expression of the placenta by Credé's method.

Mr. Gibberd then continued: For the management of hæmorrhage in the third stage of labour in the practice of a midwife acting alone, the routine treatment should not exceed two attempts at expression of the placenta. No one seriously expected a midwife to embark upon the operation of manual removal of the placenta or of bi-manual compression of the uterus without an anæsthetic. There was every reason to believe that such heroic treatment if adopted was more likely to kill the patient than to save her life. It was therefore important to cease advocating a treatment simply for traditional reasons, and more emphasis should be placed upon the importance of the general measures for combating collapse that can be applied while proper assistance is awaited.

There were three reasons, two common, and one extremely rare, for failing to express the placenta by Credé's method. The common reasons were (*a*) Mechanical difficulty in securing a satisfactory grip of the uterus (e.g. an obese abdomen); and (*b*) a contraction ring. The rare reason—the speaker himself had not met a case—was a "total" placenta accreta. Cases of "focal" placenta accreta, though not so excessively rare, did not present themselves clinically as cases of "retained placenta", but rather as cases of retained fragments of placenta. If two attempts at Credé's expression fail, the difficulty under (*a*) will not be lessened, and the difficulty under (*b*) will be increased by further attempts. However urgent the hæmorrhage may be, no other local treatment should be attempted until an anæsthetist is available and proper preparations have been made for manual exploration of the uterus. One more attempt at expression under anæsthesia should be made. If the difficulty was inaccessibility of the uterus, the anæsthesia is generally sufficient to overcome the difficulty. If the attempt at expression under anæsthesia fails, manual removal of the placenta should be embarked upon immediately. With the exception of "total" placenta accreta and of certain very rare examples of angular pregnancy, there is only one cause of mechanical difficulty in manual removal of the placenta, viz. a contraction ring. This contraction ring may, rarely, be so marked as entirely to defeat attempts at removal of the placenta. More often it causes varying degrees of difficulty on account of its cramping action on the fingers of the hand which is trying to detach the placenta. When one has, with the greatest difficulty, detached and removed a placenta, it is very easy to mistake inaccessibility for so-called "morbid adhesion". I believe "morbid adhesion" is always a mistaken diagnosis. The placenta may be very difficult to remove, but the difficulty arises, not from undue adherence of the placenta, but from the mechanical disadvantage under which a contraction ring forces anxious fingers to work. I recognize (though I have never personally met) a condition of "total" placenta accreta. There is the physiological condition of "normal adhesion" of the placenta. I am not satisfied that there is any anatomical basis, or any sufficient clinical evidence, for postulating any intermediate condition between these two extremes.

[*February* 21, 1947]

The Treatment of Tuberculous Salpingitis with Special Reference to X-ray Therapy

By Elliot Philipp, M.R.C.S., L.R.C.P.

It has been suggested to me that it might be of interest to present the results of treatment of tuberculosis of the female genital tract as carried out at the Middlesex Hospital in the past few years.

The diagnosis is not always easy, but there are said to be certain features in tuberculous salpingitis which may help one to arrive at the correct answer. The age-incidence is usually acknowledged to be between 15 and 35 years although it may occur at any age. In this series the youngest patient was 14½ years old and the oldest 36 when the condition was first diagnosed. The patient is said often to be a virgin, but 8 of this series of 20 cases were married. There may or may not be signs and symptoms usually associated with tuberculosis, such as night-sweats, loss of weight and evening rise of temperature. Amenorrhœa is sometimes present but menorrhagia is more often a symptom of the condition.

Usually the diagnosis can only be made with certainty at laparotomy: even then it is not always easy and sometimes the pathologist's report from a section of tube, omentum or other tissue removed is the first indication of the true nature of the condition.

In only one of these cases was the diagnosis made from the examination of curettings without laparotomy. This is the ideal means of diagnosis avoiding as it does laparotomy, which may light up the condition and even give rise, as in one case, to fatal issue. Of these 20 cases 13 were treated with X-rays, 7 by surgery alone. 5 of those treated by operation only were comparatively healthy women. One was treated with streptomycin and sanatorium treatment and the seventh died before X-ray therapy could be commenced. She was a girl of 23 who had complained of a swelling in the lower abdomen which had been diagnosed as an ovarian cyst and she was operated on in October 1946. On opening the abdomen a large matted mass was found and it was impossible to distinguish tubes from gut. Multiple tubercles were present. Nothing was done in the way of attempting to remove any diseased organ. The abdomen was closed and the wound appeared to be well healed after ten days. After four weeks, however, a fæcal fistula developed. The patient went downhill rapidly and died within two months.

As far as I could ascertain none of the cases treated with X-rays has relapsed and none died. But one could not be traced again after her first course of treatment and another attended follow-up for three years but has not been seen since 1944.

The X-ray treatment involves giving very small doses—a total of about 600 r in a course of twelve to eighteen treatments spread over six to nine weeks. That is, as a general working rule, two treatments a week. The dosage is small. The total is about a quarter or a third of the menopausal dose. A course may be repeated after an interval of a few months without the production of a menopause; and if there is a sinus a small dose can be given to the skin which often helps to close the sinus.

Of the 13 cases treated with X-rays 12 had had a laparotomy; 4 of these had developed a tubercular sinus, and 1 who had had hysterectomy and bilateral salpingo-oophorectomy for the condition developed a foul discharge from the cervical stump; this discharge contained tubercle bacilli. Within six months of the start of X-ray treatment all the sinuses had healed.

Periods were regular at a recent follow-up in 5 cases.

One had acquired an X-ray menopause which is unusual and undesirable; 2 had had hysterectomy, one was aged 45, another was having scanty irregular periods, and about 3 information is vague. No case had continuance of menorrhagia which is one of the commonest presenting symptoms in this series.

The case which was diagnosed on curettage only is of particular interest. In 1941 she was complaining of profuse menorrhagia. She had had tuberculous glands in her neck and a big swelling could be felt abdominally. Her temperature rose to 103°F. Histological examination of the endometrium revealed many tubercles. She received two courses of X-rays and is to-day completely symptom-free. The abdominal tumour has disappeared and she is having normal periods.

Of the cases that did not receive X-rays one had what was obviously a very chronic infection. The diagnosis was not suspected even at laparotomy and just by chance a piece of fallopian tube removed and sectioned revealed tuberculous salpingitis. She has done well.

One had pan-hysterectomy for the condition and is well.

Another who had bilateral salpingectomy and left oophorectomy for the condition complains only of dysmenorrhœa. She had two sinuses which took fifteen months to heal.

One, as recounted, died. The fifth case had bilateral salpingectomy. She is well now. Another case had an old chronic infection discovered when myomectomy was being carried out for menorrhagia. Menorrhagia has ceased.

There were three reasons, two common, and one extremely rare, for failing to express the placenta by Credé's method. The common reasons were (*a*) Mechanical difficulty in securing a satisfactory grip of the uterus (e.g. an obese abdomen); and (*b*) a contraction ring. The rare reason—the speaker himself had not met a case—was a "total" placenta accreta. Cases of "focal" placenta accreta, though not so excessively rare, did not present themselves clinically as cases of "retained placenta", but rather as cases of retained fragments of placenta. If two attempts at Credé's expression fail, the difficulty under (*a*) will not be lessened, and the difficulty under (*b*) will be increased by further attempts. However urgent the hæmorrhage may be, no other local treatment should be attempted until an anæsthetist is available and proper preparations have been made for manual exploration of the uterus. One more attempt at expression under anæsthesia should be made. If the difficulty was inaccessibility of the uterus, the anæsthesia is generally sufficient to overcome the difficulty. If the attempt at expression under anæsthesia fails, manual removal of the placenta should be embarked upon immediately. With the exception of "total" placenta accreta and of certain very rare examples of angular pregnancy, there is only one cause of mechanical difficulty in manual removal of the placenta, viz. a contraction ring. This contraction ring may, rarely, be so marked as entirely to defeat attempts at removal of the placenta. More often it causes varying degrees of difficulty on account of its cramping action on the fingers of the hand which is trying to detach the placenta. When one has, with the greatest difficulty, detached and removed a placenta, it is very easy to mistake inaccessibility for so-called "morbid adhesion". I believe "morbid adhesion" is always a mistaken diagnosis. The placenta may be very difficult to remove, but the difficulty arises, not from undue adherence of the placenta, but from the mechanical disadvantage under which a contraction ring forces anxious fingers to work. I recognize (though I have never personally met) a condition of "total" placenta accreta. There is the physiological condition of "normal adhesion" of the placenta. I am not satisfied that there is any anatomical basis, or any sufficient clinical evidence, for postulating any intermediate condition between these two extremes.

[*February* 21, 1947]

The Treatment of Tuberculous Salpingitis with Special Reference to X-ray Therapy

By Elliot Philipp, M.R.C.S., L.R.C.P.

It has been suggested to me that it might be of interest to present the results of treatment of tuberculosis of the female genital tract as carried out at the Middlesex Hospital in the past few years.

The diagnosis is not always easy, but there are said to be certain features in tuberculous salpingitis which may help one to arrive at the correct answer. The age-incidence is usually acknowledged to be between 15 and 35 years although it may occur at any age. In this series the youngest patient was 14½ years old and the oldest 36 when the condition was first diagnosed. The patient is said often to be a virgin, but 8 of this series of 20 cases were married. There may or may not be signs and symptoms usually associated with tuberculosis, such as night-sweats, loss of weight and evening rise of temperature. Amenorrhœa is sometimes present but menorrhagia is more often a symptom of the condition.

Usually the diagnosis can only be made with certainty at laparotomy: even then it is not always easy and sometimes the pathologist's report from a section of tube, omentum or other tissue removed is the first indication of the true nature of the condition.

In only one of these cases was the diagnosis made from the examination of curettings without laparotomy. This is the ideal means of diagnosis avoiding as it does laparotomy, which may light up the condition and even give rise, as in one case, to fatal issue. Of these 20 cases 13 were treated with X-rays, 7 by surgery alone. 5 of those treated by operation only were comparatively healthy women. One was treated with streptomycin and sanatorium treatment and the seventh died before X-ray therapy could be commenced. She was a girl of 23 who had complained of a swelling in the lower abdomen which had been diagnosed as an ovarian cyst and she was operated on in October 1946. On opening the abdomen a large matted mass was found and it was impossible to distinguish tubes from gut. Multiple tubercles were present. Nothing was done in the way of attempting to remove any diseased organ. The abdomen was closed and the wound appeared to be well healed after ten days. After four weeks, however, a fæcal fistula developed. The patient went downhill rapidly and died within two months.

As far as I could ascertain none of the cases treated with X-rays has relapsed and none died. But one could not be traced again after her first course of treatment and another attended follow-up for three years but has not been seen since 1944.

The X-ray treatment involves giving very small doses—a total of about 600 r in a course of twelve to eighteen treatments spread over six to nine weeks. That is, as a general working rule, two treatments a week. The dosage is small. The total is about a quarter or a third of the menopausal dose. A course may be repeated after an interval of a few months without the production of a menopause; and if there is a sinus a small dose can be given to the skin which often helps to close the sinus.

Of the 13 cases treated with X-rays 12 had had a laparotomy; 4 of these had developed a tubercular sinus, and 1 who had had hysterectomy and bilateral salpingo-oophorectomy for the condition developed a foul discharge from the cervical stump; this discharge contained tubercle bacilli. Within six months of the start of X-ray treatment all the sinuses had healed.

Periods were regular at a recent follow-up in 5 cases.

One had acquired an X-ray menopause which is unusual and undesirable; 2 had had hysterectomy, one was aged 45, another was having scanty irregular periods, and about 3 information is vague. No case had continuance of menorrhagia which is one of the commonest presenting symptoms in this series.

The case which was diagnosed on curettage only is of particular interest. In 1941 she was complaining of profuse menorrhagia. She had had tuberculous glands in her neck and a big swelling could be felt abdominally. Her temperature rose to 103°F. Histological examination of the endometrium revealed many tubercles. She received two courses of X-rays and is to-day completely symptom-free. The abdominal tumour has disappeared and she is having normal periods.

Of the cases that did not receive X-rays one had what was obviously a very chronic infection. The diagnosis was not suspected even at laparotomy and just by chance a piece of fallopian tube removed and sectioned revealed tuberculous salpingitis. She has done well.

One had pan-hysterectomy for the condition and is well.

Another who had bilateral salpingectomy and left oophorectomy for the condition complains only of dysmenorrhœa. She had two sinuses which took fifteen months to heal.

One, as recounted, died. The fifth case had bilateral salpingectomy. She is well now. Another case had an old chronic infection discovered when myomectomy was being carried out for menorrhagia. Menorrhagia has ceased.

The girl who had streptomycin has done well in spite of very small dosage. She is at a sanatorium in Switzerland. Her sinus has healed seven months after laparotomy with appendicectomy.

From all these cases the conclusion that can be drawn is that there is, as yet, no fixed rule for treatment of tuberculous tubes.

Rest, good food and heliotherapy all play their part. Though radical surgery is said to be of great value it may equally well be that surgery leads to a breakdown of protective barriers limiting the spread of the disease, to sinus formation and even to fæcal fistula. It does appear that X-ray therapy has a definite place in the condition. How the treatment works may possibly be something like this:

Small doses of X-rays traumatize tissues and destroy the most sensitive cells which are the lymphocytes. There is a general reaction to remove the destroyed cells and a very low-grade aseptic inflammation is set up which helps to overcome the tuberculous infection which previously had not been adequately combated.

I should like to thank Mr. Rivett and Mr. Winterton who operated on several of these cases and who have so kindly allowed me to use their material and also Professor Windeyer and Dr. Japha who have helped in the compilation of this paper.

Full-term Intraligamentary Pregnancy.—I. T. FRASER, F.R.C.S.Ed.

Mrs. McD., aged 26, para 0. One previous miscarriage in 1943. Admitted to University College Hospital, 3.5.46.

Last menstrual period 10.8.45. Commencing one week later, the patient had slight vaginal bleeding, and shortly afterwards experienced pain in the right lower abdomen. At 11 weeks' gestation, two pieces of "membrane" were passed, and thereafter there was a brownish vaginal discharge.

At 13 weeks' gestation the patient was admitted to Watford Peace Memorial Hospital under the care of Professor F. J. Browne. Xenopus test was positive, and she was discharged four weeks later, pregnancy continuing. At 22 weeks' gestation, the fundus was at the level of the umbilicus, but no movements had been felt. Xenopus test was now negative. At 30 weeks' gestation, fœtal heart was not heard, and X-ray examination at Watford showed the fœtus to be lying obliquely in an attitude of extreme flexion. It was thought to be dead. Some brownish discharge continued to leak vaginally. The patient was admitted to University College Hospital at 38 weeks' gestation as a case of missed abortion.

Examination showed the fundus to be 2 in. above the umbilicus. The head was felt to the left side of the fundus but was not ballotable. Fœtal heart was unexpectedly heard, rate being 120. Vaginal examination revealed fœtal limbs, felt very easily in posterior fornix.

X-ray examination showed an oblique lie of the fœtus, with such flexion of the spine that the radiologist was convinced that the fœtus was dead.

The fœtal heart continued to be satisfactorily heard, and there was a slight watery discharge *per vaginam*. A tentative attempt at version without anæsthesia was unsuccessful.

Patient experienced slight lower abdominal pains on 21.5.46, the expected date of delivery. Next day the fœtal heart had ceased. During the course of the next few weeks, two medical inductions were given without success. Further X-ray at 44 weeks' gestation showed marked collapse of the fœtal skull.

Abdominal pregnancy was considered to be a possible diagnosis. The patient was examined under anæsthesia on 2.7.46, at 46 weeks' gestation, fœtal limbs being felt with great ease in the posterior fornix. The fundus uteri could not be distinguished separately from the main swelling. A dilator passed into the uterus for 5 in., further passage not being attempted.

Laparotomy was performed. A left intraligamentary pregnancy was found, the fœtus being contained in a large ovisac, covered with fairly thick membrane and peritoneum. The uterus was enlarged and incorporated in its anterior wall. The left tube extended laterally from the uterine cornu over the sac for 3 in. before ceasing. An extension of the sac to the right contained the placenta. There were no adhesions to omentum or intestines.

The sac was opened and the fœtus removed. It was severely macerated, weighing 4 lb. There was no congenital deformity. The left ovarian ligament was divided, and the sac separated from the back of the uterus by blunt dissection. The attachment of the sac to the left side of uterus was now divided and, separating the base from the pelvis, removal was completed. The raw areas were reperitonized, and the abdomen closed.

The patient made an uninterrupted recovery and was discharged twenty-one days after operation.

Comment.—Intraligamentary pregnancy is rare. Champion and Tessitore in 1937 could find only 70 cases where such pregnancy had proceeded past the 28th week of gestation.

The apparent leakage of liquor, presumed to come from a normal uterus, was partly responsible for the delay in diagnosis. There were, however, many suggestive features—the history of pain, bleeding and of "membrane" being passed; the fixed malpresentation, uncorrectable by version, non-engagement of the presenting part and ease of feeling fœtal parts vaginally.

The attitude of the fœtus, suggesting intra-uterine death before it actually occurred, is of interest.

Had the correct diagnosis been made earlier, laparotomy before term might have resulted in a living fœtus. The high incidence of congenital abnormality in fœtuses resulting from ectopic pregnancy, noted by Von Winckel, necessitates the use of radiography to exclude this possibility, before laparotomy is carried out.

In abdominal pregnancy, which is indistinguishable from intraligamentary pregnancy before laparotomy, De Lee (1943) recommends laparotomy six weeks after term, as separation of placental adhesions to bowel may result in severe hæmorrhage in cases dealt with prior to fœtal death. However, the modern practice of leaving the placenta in situ when it is adherent to viscera has improved the results of the early operation.

REFERENCES

CHAMPION, P. K., and TESSITORE, N. J. (1937) *Amer. J. Obstet. Gynec.*, 33, 281.

DE LEE, J. B., and GREENHILL, J. P. (1943) *Principles and Practice of Obstetrics.* Philadelphia and London, 8th ed., 386.

Uterine Rupture.—IAN DONALD, M.B.

A case of uterine rupture following a previous classical Cæsarean section is not in itself remarkable but this case presented certain rather interesting features; first the rupture occurred at the end of the very last pain with which the head was born and this in the second place produced an unusual and confusing third stage, as might be expected, and thirdly a manual removal of the placenta was unwittingly carried out without the large rent in the uterus being discovered.

The patient is a healthy woman of 38 who, three years previously, at the age of 35 had a classical Cæsarean section for a breech with extended legs, her somewhat elderly primiparity being an additional indication. It is known for a fact that the uterus was sutured with interrupted catgut.

In this pregnancy the vertex presented and as there was no disproportion it was decided to allow her to proceed to natural delivery. This she achieved in 25 hours

The girl who had streptomycin has done well in spite of very small dosage. She is at a sanatorium in Switzerland. Her sinus has healed seven months after laparotomy with appendicectomy.

From all these cases the conclusion that can be drawn is that there is, as yet, no fixed rule for treatment of tuberculous tubes.

Rest, good food and heliotherapy all play their part. Though radical surgery is said to be of great value it may equally well be that surgery leads to a breakdown of protective barriers limiting the spread of the disease, to sinus formation and even to fæcal fistula. It does appear that X-ray therapy has a definite place in the condition. How the treatment works may possibly be something like this:

Small doses of X-rays traumatize tissues and destroy the most sensitive cells which are the lymphocytes. There is a general reaction to remove the destroyed cells and a very low-grade aseptic inflammation is set up which helps to overcome the tuberculous infection which previously had not been adequately combated.

I should like to thank Mr. Rivett and Mr. Winterton who operated on several of these cases and who have so kindly allowed me to use their material and also Professor Windeyer and Dr. Japha who have helped in the compilation of this paper.

Full-term Intraligamentary Pregnancy.—I. T. FRASER, F.R.C.S.Ed.

Mrs. McD., aged 26, para 0. One previous miscarriage in 1943. Admitted to University College Hospital, 3.5.46.

Last menstrual period 10.8.45. Commencing one week later, the patient had slight vaginal bleeding, and shortly afterwards experienced pain in the right lower abdomen. At 11 weeks' gestation, two pieces of "membrane" were passed, and thereafter there was a brownish vaginal discharge.

At 13 weeks' gestation the patient was admitted to Watford Peace Memorial Hospital under the care of Professor F. J. Browne. Xenopus test was positive, and she was discharged four weeks later, pregnancy continuing. At 22 weeks' gestation, the fundus was at the level of the umbilicus, but no movements had been felt. Xenopus test was now negative. At 30 weeks' gestation, fœtal heart was not heard, and X-ray examination at Watford showed the fœtus to be lying obliquely in an attitude of extreme flexion. It was thought to be dead. Some brownish discharge continued to leak vaginally. The patient was admitted to University College Hospital at 38 weeks' gestation as a case of missed abortion.

Examination showed the fundus to be 2 in. above the umbilicus. The head was felt to the left side of the fundus but was not ballotable. Fœtal heart was unexpectedly heard, rate being 120. Vaginal examination revealed fœtal limbs, felt very easily in posterior fornix.

X-ray examination showed an oblique lie of the fœtus, with such flexion of the spine that the radiologist was convinced that the fœtus was dead.

The fœtal heart continued to be satisfactorily heard, and there was a slight watery discharge *per vaginam*. A tentative attempt at version without anæsthesia was unsuccessful.

Patient experienced slight lower abdominal pains on 21.5.46, the expected date of delivery. Next day the fœtal heart had ceased. During the course of the next few weeks, two medical inductions were given without success. Further X-ray at 44 weeks' gestation showed marked collapse of the fœtal skull.

Abdominal pregnancy was considered to be a possible diagnosis. The patient was examined under anæsthesia on 2.7.46, at 46 weeks' gestation, fœtal limbs being felt with great ease in the posterior fornix. The fundus uteri could not be distinguished separately from the main swelling. A dilator passed into the uterus for 5 in., further passage not being attempted.

Laparotomy was performed. A left intraligamentary pregnancy was found, the fœtus being contained in a large ovisac, covered with fairly thick membrane and peritoneum. The uterus was enlarged and incorporated in its anterior wall. The left tube extended laterally from the uterine cornu over the sac for 3 in. before ceasing. An extension of the sac to the right contained the placenta. There were no adhesions to omentum or intestines.

The sac was opened and the fœtus removed. It was severely macerated, weighing 4 lb. There was no congenital deformity. The left ovarian ligament was divided, and the sac separated from the back of the uterus by blunt dissection. The attachment of the sac to the left side of uterus was now divided and, separating the base from the pelvis, removal was completed. The raw areas were reperitonized, and the abdomen closed.

The patient made an uninterrupted recovery and was discharged twenty-one days after operation.

Comment.—Intraligamentary pregnancy is rare. Champion and Tessitore in 1937 could find only 70 cases where such pregnancy had proceeded past the 28th week of gestation.

The apparent leakage of liquor, presumed to come from a normal uterus, was partly responsible for the delay in diagnosis. There were, however, many suggestive features—the history of pain, bleeding and of "membrane" being passed; the fixed malpresentation, uncorrectable by version, non-engagement of the presenting part and ease of feeling fœtal parts vaginally.

The attitude of the fœtus, suggesting intra-uterine death before it actually occurred, is of interest.

Had the correct diagnosis been made earlier, laparotomy before term might have resulted in a living fœtus. The high incidence of congenital abnormality in fœtuses resulting from ectopic pregnancy, noted by Von Winckel, necessitates the use of radiography to exclude this possibility, before laparotomy is carried out.

In abdominal pregnancy, which is indistinguishable from intraligamentary pregnancy before laparotomy, De Lee (1943) recommends laparotomy six weeks after term, as separation of placental adhesions to bowel may result in severe hæmorrhage in cases dealt with prior to fœtal death. However, the modern practice of leaving the placenta in situ when it is adherent to viscera has improved the results of the early operation.

REFERENCES

Champion, P. K., and Tessitore, N. J. (1937) *Amer. J. Obstet. Gynec.*, 33, 281.
De Lee, J. B., and Greenhill, J. P. (1943) Principles and Practice of Obstetrics. Philadelphia and London, 8th ed., 386.

Uterine Rupture.—Ian Donald, M.B.

A case of uterine rupture following a previous classical Cæsarean section is not in itself remarkable but this case presented certain rather interesting features; first the rupture occurred at the end of the very last pain with which the head was born and this in the second place produced an unusual and confusing third stage, as might be expected, and thirdly a manual removal of the placenta was unwittingly carried out without the large rent in the uterus being discovered.

The patient is a healthy woman of 38 who, three years previously, at the age of 35 had a classical Cæsarean section for a breech with extended legs, her somewhat elderly primiparity being an additional indication. It is known for a fact that the uterus was sutured with interrupted catgut.

In this pregnancy the vertex presented and as there was no disproportion it was decided to allow her to proceed to natural delivery. This she achieved in 25 hours

The girl who had streptomycin has done well in spite of very small dosage. She is at a sanatorium in Switzerland. Her sinus has healed seven months after laparotomy with appendicectomy.

From all these cases the conclusion that can be drawn is that there is, as yet, no fixed rule for treatment of tuberculous tubes.

Rest, good food and heliotherapy all play their part. Though radical surgery is said to be of great value it may equally well be that surgery leads to a breakdown of protective barriers limiting the spread of the disease, to sinus formation and even to fæcal fistula. It does appear that X-ray therapy has a definite place in the condition. How the treatment works may possibly be something like this:

Small doses of X-rays traumatize tissues and destroy the most sensitive cells which are the lymphocytes. There is a general reaction to remove the destroyed cells and a very low-grade aseptic inflammation is set up which helps to overcome the tuberculous infection which previously had not been adequately combated.

I should like to thank Mr. Rivett and Mr. Winterton who operated on several of these cases and who have so kindly allowed me to use their material and also Professor Windeyer and Dr. Japha who have helped in the compilation of this paper.

Full-term Intraligamentary Pregnancy.—I. T. FRASER, F.R.C.S.Ed.

Mrs. McD., aged 26, para 0. One previous miscarriage in 1943. Admitted to University College Hospital, 3.5.46.

Last menstrual period 10.8.45. Commencing one week later, the patient had slight vaginal bleeding, and shortly afterwards experienced pain in the right lower abdomen. At 11 weeks' gestation, two pieces of "membrane" were passed, and thereafter there was a brownish vaginal discharge.

At 13 weeks' gestation the patient was admitted to Watford Peace Memorial Hospital under the care of Professor F. J. Browne. Xenopus test was positive, and she was discharged four weeks later, pregnancy continuing. At 22 weeks' gestation, the fundus was at the level of the umbilicus, but no movements had been felt. Xenopus test was now negative. At 30 weeks' gestation, fœtal heart was not heard, and X-ray examination at Watford showed the fœtus to be lying obliquely in an attitude of extreme flexion. It was thought to be dead. Some brownish discharge continued to leak vaginally. The patient was admitted to University College Hospital at 38 weeks' gestation as a case of missed abortion.

Examination showed the fundus to be 2 in. above the umbilicus. The head was felt to the left side of the fundus but was not ballotable. Fœtal heart was unexpectedly heard, rate being 120. Vaginal examination revealed fœtal limbs, felt very easily in posterior fornix.

X-ray examination showed an oblique lie of the fœtus, with such flexion of the spine that the radiologist was convinced that the fœtus was dead.

The fœtal heart continued to be satisfactorily heard, and there was a slight watery discharge *per vaginam*. A tentative attempt at version without anæsthesia was unsuccessful.

Patient experienced slight lower abdominal pains on 21.5.46, the expected date of delivery. Next day the fœtal heart had ceased. During the course of the next few weeks, two medical inductions were given without success. Further X-ray at 44 weeks' gestation showed marked collapse of the fœtal skull.

Abdominal pregnancy was considered to be a possible diagnosis. The patient was examined under anæsthesia on 2.7.46, at 46 weeks' gestation, fœtal limbs being felt with great ease in the posterior fornix. The fundus uteri could not be distinguished separately from the main swelling. A dilator passed into the uterus for 5 in., further passage not being attempted.

Section of Epidemiology and State Medicine

President—H. J. PARISH, M.D.

[*November* 22, 1946]

DISCUSSION: MODERN METHODS IN THE CONTROL OF AIRBORNE INFECTIONS [*Abridged*]

Dr. R. Cruickshank: Airborne infection may be defined as infection by inhalation and includes many of the specific fevers besides respiratory infections proper. The present incidence of airborne infection is high. Although the *mortality* due to measles and whooping-cough has fallen steadily during the last fifty years their *prevalence* is probably as great as it was a century ago. It is likely also that there has been no diminution in the incidence of the less well-defined "acute respiratory diseases" such as colds, febrile catarrh and influenza and their secondary complications. In America members of widely different social and geographical groups have been found to have on an average three colds a year. In Great Britain several investigations have shown that 40 to 50% of the time lost from work or school is due to acute respiratory infections including influenza (Smith, 1934, two communities in Glasgow; Report, 1938, children in boarding schools; Report, 1946*a*, adults in wartime). These infections are therefore a source of great economic loss.

Community foci from which respiratory diseases may be introduced into the family are the school; the day nursery (Report, 1946*b*); the train, tube or bus; the office or factory; and the cinema or other place of entertainment. The risk of infection in such places can be estimated by bacteriological sampling of the air using *Strep. viridans* as an index of pollution (Buchbinder *et al.*, 1938). The detection of tracer substances volatilized in the air (Lidwell and Lovelock, 1946) allows frequent measurements of ventilation rates. There is need for correlation of these methods with careful sickness records among workers in a factory or large institution.

The relative importance of droplets, dust and droplet nuclei in the spread of infection is best assessed by eliminating one variable and noting the effect on the cross-infection rate. Spread by direct droplets is contact rather than airborne infection. It is perhaps not very important in streptococcal infections because throat carriers of hæmolytic streptococci do not expel many organisms when they cough or talk (Hare and Mackenzie, 1946). However, the classical experiments of Dr. Alison Glover on the control of epidemic cerebrospinal fever showed the value of reducing the risk of droplet spread by increasing the space between adjacent beds. Similar measures reduced by 50% the epidemic incidence of acute respiratory disease in new recruits in the American Army (Commission on Acute Respiratory Disease, 1946*a*).

Infected dust was shown to be important when the incidence of streptococcal cross-infection rate. Spread by direct droplets is contact rather than airborne dust control developed in England by van den Ende and his colleagues. Nasal carriers of hæmolytic streptococci appear to be the most important contributors to infection of the environment (Hamburger *et al.*, 1945, 1946). On the other hand dust-control measures did not prevent the epidemic spread of acute respiratory disease among troops in training (Commission on Acute Respiratory Diseases, 20 minutes of which only 1 hour 20 minutes were spent in an easy second stage. The very last pain was a strong one which both crowned and delivered the head in one, the shoulders and body being then extracted. The child, which was stillborn, weighed 7 lb.

Within two minutes the patient became profoundly shocked although no blood appeared at the vulva. The pulse disappeared at the wrist and the blood-pressure sank to 60/?.

Her condition was far too critical to do anything more than institute resuscitative measures. She was accordingly given oxygen, morphia and heat and the foot of the bed was raised and transfusion first with plasma and then with whole blood was commenced at maximum delivery rate both into the arm and leg.

From the time of the onset of the shock the abdomen was acutely tender and the fundus could not be felt and at no time was there any external bleeding and moreover the whole surface of the abdomen was resonant on percussion. Acute inversion seemed therefore the most likely diagnosis.

After two hours her condition had rallied sufficiently to warrant internal examination, the systolic blood-pressure being now just over 100. Accordingly an anæsthetic was administered.

On introducing the hand into the vagina a most peculiar elliptical slit was felt in the region of the cervix through which the hand could not be passed until a capsule of amyl nitrite had been broken under the anæsthetic mask. Following this the hand was able to follow the cord into the uterus where the placenta was found completely unseparated. It was of the battledore variety and was removed completely. A certain amount of bleeding accompanied this manœuvre but the uterus was rubbed up until a good contraction was secured and maintained with ergometrine and further bleeding *per vaginam* ceased.

The transfusion was continued and one and a half hours after the removal of the placenta she had had in all 2 pints of plasma and 4 pints of blood; she looked less pale, her pulse was 100 and her blood-pressure 115/75 but on examining her the fundus could not be felt and yet there was no sign of any bleeding *per vaginam*. Moreover, for a woman who had just received so much blood her condition was not good. Some fullness was noticed in the flanks and she complained of pain across both shoulders, especially the right. On percussion there was unmistakable dullness in the flanks. The abdomen felt doughy but the physical signs had been obscured by the administration of morphia.

A diagnosis of ruptured uterus was made with hæmoperitoneum, and laparotomy was forthwith undertaken. The peritoneal cavity was found indeed to contain a very large quantity of blood and the uterus was found to have ruptured throughout the entire length of the previous Cæsarean section scar.

Subtotal hysterectomy was rapidly carried out and the patient made an uninterrupted recovery. Total transfusion amounted to 8½ pints.

The section shows chorionic villi in relation with the ruptured scar, with large areas of fibrous tissue much of which is very degenerate.

I would like to thank Dr. Wrigley for permission to describe this case and also for the help and moral support which he gave at the time.

Section of Epidemiology and State Medicine

President—H. J. Parish, M.D.

[*November* 22, 1946]

DISCUSSION: MODERN METHODS IN THE CONTROL OF AIRBORNE INFECTIONS [*Abridged*]

Dr. R. Cruickshank: Airborne infection may be defined as infection by inhalation and includes many of the specific fevers besides respiratory infections proper. The present incidence of airborne infection is high. Although the *mortality* due to measles and whooping-cough has fallen steadily during the last fifty years their *prevalence* is probably as great as it was a century ago. It is likely also that there has been no diminution in the incidence of the less well-defined "acute respiratory diseases" such as colds, febrile catarrh and influenza and their secondary complications. In America members of widely different social and geographical groups have been found to have on an average three colds a year. In Great Britain several investigations have shown that 40 to 50% of the time lost from work or school is due to acute respiratory infections including influenza (Smith, 1934, two communities in Glasgow; Report, 1938, children in boarding schools; Report, 1946*a*, adults in wartime). These infections are therefore a source of great economic loss.

Community foci from which respiratory diseases may be introduced into the family are the school; the day nursery (Report, 1946*b*); the train, tube or bus; the office or factory; and the cinema or other place of entertainment. The risk of infection in such places can be estimated by bacteriological sampling of the air using *Strep. viridans* as an index of pollution (Buchbinder *et al.*, 1938). The detection of tracer substances volatilized in the air (Lidwell and Lovelock, 1946) allows frequent measurements of ventilation rates. There is need for correlation of these methods with careful sickness records among workers in a factory or large institution.

The relative importance of droplets, dust and droplet nuclei in the spread of infection is best assessed by eliminating one variable and noting the effect on the cross-infection rate. Spread by direct droplets is contact rather than airborne infection. It is perhaps not very important in streptococcal infections because throat carriers of hæmolytic streptococci do not expel many organisms when they cough or talk (Hare and Mackenzie, 1946). However, the classical experiments of Dr. Alison Glover on the control of epidemic cerebrospinal fever showed the value of reducing the risk of droplet spread by increasing the space between adjacent beds. Similar measures reduced by 50% the epidemic incidence of acute respiratory disease in new recruits in the American Army (Commission on Acute Respiratory Disease, 1946*a*).

Infected dust was shown to be important when the incidence of streptococcal cross-infection rate. Spread by direct droplets is contact rather than airborne dust control developed in England by van den Ende and his colleagues. Nasal carriers of hæmolytic streptococci appear to be the most important contributors to infection of the environment (Hamburger *et al.*, 1945, 1946). On the other hand dust-control measures did not prevent the epidemic spread of acute respiratory disease among troops in training (Commission on Acute Respiratory Diseases, 20 minutes of which only 1 hour 20 minutes were spent in an easy second stage. The very last pain was a strong one which both crowned and delivered the head in one, the shoulders and body being then extracted. The child, which was stillborn, weighed 7 lb.

Within two minutes the patient became profoundly shocked although no blood appeared at the vulva. The pulse disappeared at the wrist and the blood-pressure sank to 60/?.

Her condition was far too critical to do anything more than institute resuscitative measures. She was accordingly given oxygen, morphia and heat and the foot of the bed was raised and transfusion first with plasma and then with whole blood was commenced at maximum delivery rate both into the arm and leg.

From the time of the onset of the shock the abdomen was acutely tender and the fundus could not be felt and at no time was there any external bleeding and moreover the whole surface of the abdomen was resonant on percussion. Acute inversion seemed therefore the most likely diagnosis.

After two hours her condition had rallied sufficiently to warrant internal examination, the systolic blood-pressure being now just over 100. Accordingly an anæsthetic was administered.

On introducing the hand into the vagina a most peculiar elliptical slit was felt in the region of the cervix through which the hand could not be passed until a capsule of amyl nitrite had been broken under the anæsthetic mask. Following this the hand was able to follow the cord into the uterus where the placenta was found completely unseparated. It was of the battledore variety and was removed completely. A certain amount of bleeding accompanied this manœuvre but the uterus was rubbed up until a good contraction was secured and maintained with ergometrine and further bleeding *per vaginam* ceased.

The transfusion was continued and one and a half hours after the removal of the placenta she had had in all 2 pints of plasma and 4 pints of blood; she looked less pale, her pulse was 100 and her blood-pressure 115/75 but on examining her the fundus could not be felt and yet there was no sign of any bleeding *per vaginam*. Moreover, for a woman who had just received so much blood her condition was not good. Some fullness was noticed in the flanks and she complained of pain across both shoulders, especially the right. On percussion there was unmistakable dullness in the flanks. The abdomen felt doughy but the physical signs had been obscured by the administration of morphia.

A diagnosis of ruptured uterus was made with hæmoperitoneum, and laparotomy was forthwith undertaken. The peritoneal cavity was found indeed to contain a very large quantity of blood and the uterus was found to have ruptured throughout the entire length of the previous Cæsarean section scar.

Subtotal hysterectomy was rapidly carried out and the patient made an uninterrupted recovery. Total transfusion amounted to 8½ pints.

The section shows chorionic villi in relation with the ruptured scar, with large areas of fibrous tissue much of which is very degenerate.

I would like to thank Dr. Wrigley for permission to describe this case and also for the help and moral support which he gave at the time.

little killing at low concentrations, then a rapid increase and finally a relatively constant maximum. (2) Relative humidity exerts a dominant effect giving maximum killing between 60% and 80%. A rapid fall in killing rate below 50% relative humidity considerably reduces the effectiveness under many working conditions. (3) Increase in particle size diminishes the killing rate. (4) The nature of the particles also affects the rate, which is low with dry dust particles, intermediate with natural sprayed salivary flora, and very high with sprayed cultures. Different species of organisms vary in sensitivity. In field trials most airborne organisms are dry, dust-borne and resistant.

Dr. M. Mitman had found that a germicidal mist of resorcinol generated in a cubicle by a simple apparatus, the aerovap, failed to give significant reduction in the numbers of organisms and hæmolytic streptococci falling on exposed plates. Nevertheless, he felt that intermittent aerial disinfection at the times of activities known to cause peak infection would be a valuable method of preventing spread of infection from cubicle to corridor.

Major A. C. Cunliffe described an experiment which was made during an outbreak of infection with *Strep. pyogenes*, types 4 and 12, in a ward of children undergoing plastic operations of the palate, in which oil-treatment of the bed-clothes was associated with a marked reduction in the numbers of airborne streptococci and a significant decrease in the cross-infection rate. In the six weeks before the application of oiled bed-clothes the average number of *Strep. pyogenes* isolated by a slit sampler during bed-making was 22·6 ± 8·1 per cu. ft. of air, while all 16 post-operative patients were found at routine swabbings to have acquired *Strep. pyogenes* (a cross-infection rate of 100%). In the following nineteen days when all bed-clothes were oil-treated, the average number of streptococci was 0·7 ± 0·24; 5 (41·7%) of 12 patients were cross-infected. In the next three weeks when unoiled bed-clothes were used the average number of streptococci rose to 2·7 ± 0·8 and 70·6% of 17 patients were cross-infected.

Dr. J. L. Burn showed photographs illustrating some points in the prevention of airborne infection in schools and day nurseries.

Dr. J. M. Alston did not agree that acute respiratory disease could be attributed entirely to airborne infection. Endogenous infection and contact spread were important, and contaminated hands and handkerchiefs probably played a large part. Impregnation of handkerchiefs with penicillin or other antibacterial substance seemed worth experiment.

Dr. William Gunn commented on Dr. Wright's results and conclusions stressing that significant differences between test and control groups could be expected only when atmospheric contamination was high. Under present conditions a certain amount of infection was to be expected especially in highly susceptible children. Oiling of floors and fabrics was the only practicable method available for suppressing dust.

Professor Ronald Hare said that in United States Army and Navy barracks ultraviolet light and triethylene glycol aerosols had failed to produce any dramatic reduction in upper respiratory tract infections. Prevention of a very infectious virus disease such as influenza might be much more difficult than prevention of a microbic infection such as scarlet fever. Wide variations of attack rates occurred in comparable groups of persons without control measures, and therefore prolonged investigations would be necessary before any particular prophylactic could be said to have achieved its object.

1946*b*). Therefore spread by dust may be more important in bacterial than in virus infections.

Droplet nuclei are probably the usual mode of spread of virus infections where the infecting dose is small. Control of droplet nuclei by ultraviolet light has been achieved in America in the case of measles in school classrooms (Wells, Wells and Wilder, 1942) and of respiratory infections in infants at the Cradle Hospital.

The application of new methods of attack on the channels of airborne infection is enlightening the darkness that envelops this complex problem and we may take pride in the knowledge that many of the advances have originated from work done in this country.

REFERENCES

BUCHBINDER, L., SOLOWEY, M., and SOLOTOROVSKY, M. (1938) *Amer. J. publ. Hlth.*, 28, 61.
Commission on Acute Respiratory Diseases (1946*a*) *Amer. J. Hyg.*, 43, 65.
—— (1946*b*) *Amer. J. Hyg.*, 43, 120.
HAMBURGER, M., GREEN, M. J., and HAMBURGER, V. (1945) *J. infect. Dis.*, 77, 96.
——, and LEMON, H. M. (1946) *J. Amer. med. Ass.*, 130, 836.
HARE, R., and MACKENZIE, D. M. (1946) *Brit. med. J.* (i), 865.
LIDWELL, O. M., and LOVELOCK, J. E. (1946) *J. Hyg., Camb.*, 44, 326.
Report (1938) School Epidemics Committee. *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 227.
Report (1946*a*) C.M.O. Min. Hlth. On the State of the Public Health during Six Years of War.
Report (1946*b*) Day Nurseries Committee of Med. Women's Fedn., *Brit. med. J.*, (ii), 217.
SMITH, C. M. (1934) *Spec. Rep. Ser. med. Res. Coun., Lond.*, No. 192.
WELLS, W. F., WELLS, M. W., and WILDER, T. S. (1942) *Amer. J. Hyg.*, 35, 97.

Dr. Joyce Wright discussed two trials of dust-control measures in measles wards. In the first trial (Wright *et al.*, 1944) oiling of blankets, bed linen, garments and floors in one ward reduced the bacterial and hæmolytic streptococcal counts of the air during bed-making to 91% and 98% respectively below those in a control ward. The streptococcal cross-infection rate was lower in the oiled ward than in the control (18·6 *versus* 73·3%) as was the rate of otorrhœa due to streptococcal cross-infection (2·8 *v.* 14·3%). Most cross-infections were due to type 6 streptococci. In the second trial (Begg *et al.*, 1947) bacterial counts in the control ward were low and there was less difference between them and counts in the oiled ward. The streptococcal cross-infection rate was higher in the oiled ward than in the control ward (20·5 *v.* 12·4%). The cross-infections were due to different types of streptococci and probably to contact spread. More cases with skin sepsis and streptococcal otorrhœa were admitted to the oiled than to the control ward despite alternate allocation of new patients. Dust-suppressive measures may be useful in measles wards if there is a high incidence of streptococcal infection.

REFERENCES

BEGG, N. D., SMELLIE, E. W., and WRIGHT, J. (1947) *Brit. med. J.* (i), 209.
WRIGHT, J., CRUICKSHANK, R., and GUNN, W. (1944) *Brit. med. J.* (i), 611.

Mr. F. Courtney Harwood emphasized that good laundering methods are essential if oiling of fabrics is to be satisfactory. Oiling is a simple process if goods are washed and rinsed and softened water is used. Blankets can be steam sterilized without loss of oil. He said that research into laundering methods was continuing.

Dr. O. M. Lidwell discussed the results of laboratory tests of α-hydroxy-carboxylic acids as aerial disinfectants. Details will be published elsewhere. The bactericidal effect can be represented by a logarithmic killing curve and calculated as "equivalent air changes per hour." The resultant reduction of the contamination of air in a room depends on the pre-existing rate of removal of bacteria-carrying particles by ventilation and sedimentation. In order to halve the mean concentration of bacteria-carrying particles, it is necessary to double the overall rate of removal.

Four important factors affect the killing rate of α-hydroxy-carboxylic acids. (1) Increase in concentration of the bactericide usually gives an S-shaped curve with little killing at low concentrations, then a rapid increase and finally a relatively constant maximum. (2) Relative humidity exerts a dominant effect giving maximum killing between 60% and 80%. A rapid fall in killing rate below 50% relative humidity considerably reduces the effectiveness under many working conditions. (3) Increase in particle size diminishes the killing rate. (4) The nature of the particles also affects the rate, which is low with dry dust particles, intermediate with natural sprayed salivary flora, and very high with sprayed cultures. Different species of organisms vary in sensitivity. In field trials most airborne organisms are dry, dust-borne and resistant.

Dr. M. Mitman had found that a germicidal mist of resorcinol generated in a cubicle by a simple apparatus, the aerovap, failed to give significant reduction in the numbers of organisms and hæmolytic streptococci falling on exposed plates. Nevertheless, he felt that intermittent aerial disinfection at the times of activities known to cause peak infection would be a valuable method of preventing spread of infection from cubicle to corridor.

Major A. C. Cunliffe described an experiment which was made during an outbreak of infection with *Strep. pyogenes*, types 4 and 12, in a ward of children undergoing plastic operations of the palate, in which oil-treatment of the bed-clothes was associated with a marked reduction in the numbers of airborne streptococci and a significant decrease in the cross-infection rate. In the six weeks before the application of oiled bed-clothes the average number of *Strep. pyogenes* isolated by a slit sampler during bed-making was 22·6 ± 8·1 per cu. ft. of air, while all 16 post-operative patients were found at routine swabbings to have acquired *Strep. pyogenes* (a cross-infection rate of 100%). In the following nineteen days when all bed-clothes were oil-treated, the average number of streptococci was 0·7 ± 0·24; 5 (41·7%) of 12 patients were cross-infected. In the next three weeks when unoiled bed-clothes were used the average number of streptococci rose to 2·7 ± 0·8 and 70·6% of 17 patients were cross-infected.

Dr. J. L. Burn showed photographs illustrating some points in the prevention of airborne infection in schools and day nurseries.

Dr. J. M. Alston did not agree that acute respiratory disease could be attributed entirely to airborne infection. Endogenous infection and contact spread were important, and contaminated hands and handkerchiefs probably played a large part. Impregnation of handkerchiefs with penicillin or other antibacterial substance seemed worth experiment.

Dr. William Gunn commented on Dr. Wright's results and conclusions stressing that significant differences between test and control groups could be expected only when atmospheric contamination was high. Under present conditions a certain amount of infection was to be expected especially in highly susceptible children. Oiling of floors and fabrics was the only practicable method available for suppressing dust.

Professor Ronald Hare said that in United States Army and Navy barracks ultraviolet light and triethylene glycol aerosols had failed to produce any dramatic reduction in upper respiratory tract infections. Prevention of a very infectious virus disease such as influenza might be much more difficult than prevention of a microbic infection such as scarlet fever. Wide variations of attack rates occurred in comparable groups of persons without control measures, and therefore prolonged investigations would be necessary before any particular prophylactic could be said to have achieved its object.

[*January* 24, 1947]

Whooping Cough and Measles

An Epidemiological Concurrence and Contrast

By WILLIAM BUTLER, M.B.
(*Brevet Lieut.-Colonel, Retd.*)

THERE is an intimate association of whooping cough and measles. They are coupled in the popular mind as affections of childhood, normally to be expected almost as inevitably as those of teething. Familiarity had bred a contempt which their comparatively low case fatality appeared to condone and yet at the time when this contempt most prevailed their respective contributions to child mortality were each of them higher than those of any other infectious disease. One hundred years ago, whooping cough exacted on an average each year in round figures 500 deaths per million population and measles over 400, to-day their mortality has fallen respectively to about 30 per million. The decline in mortality set in earlier in the case of whooping cough and its quinquennial rates have been uninterrupted in their progressive fall during a period of over 60 years. Measles, which lagged in its decline until the beginning of the present century and at the beginning was less steady in its fall, has nevertheless during the last quarter of a century sustainedly reduced the lead until now the respective annual mortality contributions are about equal. It has long been noted that the mortality among females was higher than that of males in whooping cough and lower in measles. The decline throughout a prolonged period in mortality for each sex in both diseases has maintained the respective sex ratios, though if the crude death-rates of each sex at all ages be taken, the positions with regard both to measles and whooping cough are reversed in the years of the first Great War.

Batch fatality rates.—It is an obvious advantage to have recorded the case fatalities from current diseases continuously throughout the period of their occurrence. A rate relating deaths to the actual cases from which they derive, where that is possible, is the most reliable statement of case fatality.

The batch fatality rate computed by the method described in a paper on "The Fatality Rate of Measles" (*J. R. statist. Soc.*, 1945, **108**, Pts. 3 and 4) gives, I believe, a very close approximation to this result. It is true of the batch fatality rates advancing *seriatim* week by week with the returns that they assume the character of a moving average picking up belated deaths and dropping others which later are ascribed as fatalities of subsequent batches. This has the effect of slightly flattening the curves described by the varying rates but, if the pre-fatal interval obtains in anything like the proportions I have assumed on the bases of the somewhat limited analysis which has been available, the instances which do not strictly belong to the batch period must be very few in number. In any case, the rates do exhibit, very closely to what is actually occurring, fluctuations which with the same approximate accuracy are shown by no other method with which I am acquainted.

In an analysis made between thirty and forty years ago of 196 deaths from measles and of 187 deaths from whooping cough I found that while in measles 93% of the deaths had occurred by the end of four weeks from onset, only 75% of the deaths from whooping cough had occurred within that period. For this and for other reasons I considered that in the case of measles it was sufficiently near the facts to assume that if a fatal termination were to occur it would do so within five weeks of onset, which gave a batch period of nine weeks and a fatality term of five weeks and on this assumption the formula for calculating the batch fatality rate was constructed (*J. R. statist. Soc.*, 1945, **108**, Pts. 3 and 4). The error in the case of measles was negligible so far as the few cases dying outside these limits was concerned. In the case of whooping cough the difficulty of determining a period within which all fatalities would occur was greater. 25% of the fatalities occurred beyond the fourth week of onset of the disease and it is practically certain that not all—if even the greater part—of the remaining fatal cases would die within another week as might be practically assumed of the smaller residue in the case of measles. On the other hand the further the batch period was extended beyond that within which the bulk of the remaining fatalities actually occurred, the less definite was the relationship of the batch to the deaths to which it was presumed they were specifically related. Moreover, the deaths ascribed to whooping cough are more inclusive of all fatalities from this disease than are the returns of measles of the actual cases of death from morbilli, and for this reason: the chief causes of death from either of these affections are pulmonary complications. The diagnostic evidences of measles disappear with the eruption but those of whooping cough obtrude themselves for weeks after the onset of the disease. As a result pulmonary affections are recognized as secondary in higher proportion in the case of whooping cough: in measles the primary affection may never have been recognized, its diagnostic evidences having disappeared before medical aid was sought. It follows that the number of cases of whooping cough dying at the more remote periods from onset are recognized as such in greater proportion than in the case of measles. In assuming that whooping cough has a six weeks' fatality term, necessary for practical purposes, it has to be recognized that a higher, though relatively a small, proportion of the deaths which should be totalled in the six weeks' fatality term from cases occurring during the batch period of eleven weeks are carried over and included in succeeding fatality terms. This has the effect greater than in the case of measles of slightly flattening the curve of case fatality rates. Nevertheless it remains approximately correct and is a useful, though not an exact, figure. The batch fatality rates of measles and of whooping cough have been calculated for each week over the six complete years, 1940-45, during which these diseases have been notifiable (Table I). They are based on the Registrar-General's returns for London and the Great Towns and the respective formulæ used were:—

FORMULA FOR CALCULATING BATCH FATALITY RATES

Where serial cases and deaths are recorded week by week as in the Registrar-General's weekly returns of notifications, the batch fatality rate at the terminal week of each successive—Measles: 9-weekly, whooping cough: 11-weekly—period is:—

MEASLES

$$\frac{\text{The sum of the deaths during last five weeks} \times 1{,}000}{\text{(Half the sum of the cases of the first four weeks + all the cases of the middle week + half the sum of the cases of the last four weeks)}}$$

WHOOPING COUGH

$$\frac{\text{The sum of the deaths during last six weeks} \times 1{,}000}{\text{(Half the sum of the cases of the first five weeks + all the cases of the middle week + half the sum of the cases of the last five weeks)}}$$

TABLE I.—MONTHLY AVERAGES OF BATCH FATALITY RATES PER 1,000, LONDON AND GREAT TOWNS.

	Measles						Mean of monthly averages 6 years	Whooping cough						Mean of monthly averages 6 years	Whooping cough. Multiples of measles B.F.R.	
	1940	1941	1942	1943	1944	1945		1940	1941	1942	1943	1944	1945			
Jan. ..	4·1	3·4	1·7	2·4	2·9	2·6	2·8	13·0	15·8	14·2	15·3	15·7	17·5	15·2	6·0	5·0
Feb. ..	5·4	3·9	2·6	2·4	1·3	2·1	2·9	29·4	22·5	14·8	16·8	14·0	18·6	19·3		6·6
March ..	3·2	3·7	3·4	2·7	2·1	2·1	2·9	30·0	22·9	13·1	14·7	11·3	13·1	17·5		6·1
April ..	2·1	3·9	2·3	2·5	1·4	1·7	2·6	28·1	20·2	16·3	14·4	11·3	11·7	17·0		6·5
May ..	2·2	2·7	2·3	1·8	1·8	1·4	2·0	19·3	15·4	16·2	12·4	13·4	10·7	14·5	7·2	7·2
June ..	1·6	2·5	2·4	1·2	1·4	1·2	1·7	10·8	13·6	11·8	10·6	14·1	9·4	11·7		6·9
July ..	1·7	2·1	1·4	0·6	1·1	1·2	1·3	12·4	13·4	9·3	8·4	10·8	5·9	10·2		7·5
Aug. ..	1·6	1·4	1·2	1·3	1·6	0·8	1·3	8·9	12·0	8·7	8·5	10·6	8·0	9·4		7·3
Sept. ..	2·5	1·8	1·0	2·6	0·8	1·6	1·7	10·3	11·2	11·0	10·5	9·5	8·1	10·1	4·8	5·7
Oct. ..	3·4	3·0	2·0	2·7	1·8	1·6	2·4	13·9	11·0	14·4	12·3	13·8	8·0	12·2		5·1
Nov. ..	4·0	4·1	1·8	3·4	2·4	4·0	3·3	15·0	9·3	12·7	10·4	11·9	9·0	11·4		3·5
Dec. ..	2·7	3·1	2·2	3·2	2·6	1·9	2·6	12·0	10·4	14·3	15·3	13·7	13·0	13·1		5·0
Mean Annual ..	2·9	3·0	1·9	2·2	1·8	1·9	2·3	16·9	14·7	13·6	12·5	12·5	11·1	13·5		
Mean of two years	2·9		2·0		1·9		2·3	15·8		13·0		11·8		13·5		
Whooping cough. Multiple of measles B.F.R.								5·8	4·9	7·2	5·7	6·9	5·9			
								5·4 times		6·5 times		6·2 times				

Seasonal variations in fatality.—Perhaps the most outstanding feature of the batch fatality rates as well of measles as of whooping cough is the regular, and in the uniformity of behaviour, definitely characteristic variations with season.

As will be seen from Table I and fig. 1 there is a close correspondence in the seasonal variations of fatality in the two diseases. In both, fatality is lowest in the warmer months of the year. Measles falls below the mean earlier (May) than whooping cough (June) and the case fatality of whooping cough appears to be less adversely affected by late autumn than that of measles.

EXPLANATION OF GRAPHS

The graphs are of the differences, expressed as a percentage above or below the six-yearly mean, between the weekly numbers of cases averaged for each month and the weekly numbers of cases averaged for six years. The course of incidence, just as if of the actual monthly mean of weekly numbers, is shown in three successive biennial periods, either singly for each biennial span or by superimposition of three successive biennial graphs. The composite graphs are of the means of the cases so graphed and respectively comprised in the three successive biennial periods.

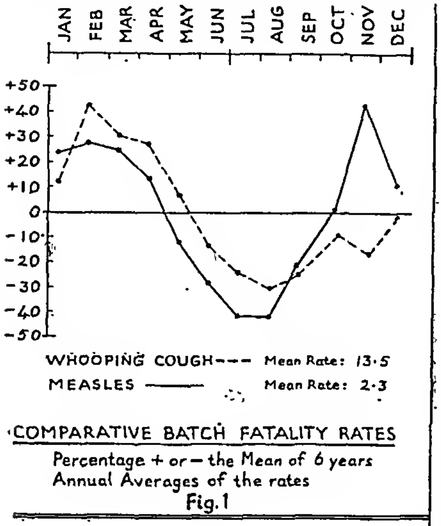


FIG. 1.

MEASLES

Fig. 5. Superimposed biennial distribution — 6 years →

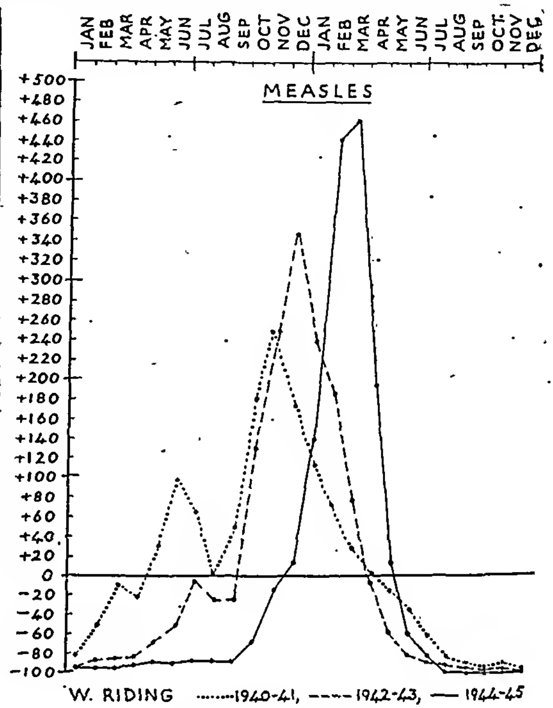


FIG. 5 (*see also* fig. 4).

Taking consecutive months in each third of the year, the four months, May to August, are more favourable to measles than to whooping cough which, in its batch fatality rates averaged for the period, has a multiple 7·2 times the batch fatality rates similarly averaged for measles. The first four months of the year are next more favourable to measles with a whooping cough ratio 6·0 times the average batch fatality rates of measles, while in the last four months, measles is relatively much more adversely affected, the multiple of whooping cough to measles average batch fatality rates falling to 4·8 times.

In Table II are set out the maximal and minimal rates among the serial batches of each year and the months in which they occurred:

TABLE II.—WHOOPING COUGH AND MEASLES MAXIMUM AND MINIMUM BATCH FATALITY RATES PER 1,000.

		Maximum during year	Month of occurrence	Minimum during year	Month of occurrence	The averaged mean of monthly B.F.R.s each year
1940	Whooping cough	32·9	February	8·1	August	16·9
	Measles	6·4	November	1·4	August	2·9
1941	,,	23·8	February	8·3	December	14·7
	,,	4·3	November	1·2	August	3·0
1942	,,	18·0	May	7·8	August	13·6
	,,	4·2	February	1·0	September	1·9
1943	,,	17·3	March	7·6	July	12·5
	,,	4·7	October	0·4	July	2·2
1944	,,	15·8	January	8·7	September	12·5
	,,	4·6	January	0·3	September	1·8
1945	,,	20·1	February	5·3	July	11·1
	,,	5·8	November	0·2	August	1·9

Yearly decline in case fatality.—Throughout the six years, the batch fatality rates both of measles and of whooping cough are unexpectedly low. The continuing decline from previously accepted rates to the low figures of the notification years is still to be observed as a process common to both diseases. During the notification period the measles batch fatality rate has declined by about one-third, that of whooping cough by about one-fourth.

If we turn from batch fatality rates to case fatality calculated on the annual totals of cases and deaths from either disease during each successive year, confirmation of this trend is disclosed and the behaviour of the rates not only of London and the Great Towns but of England and Wales also can be observed (Table III). Although case fatality rates calculated on these data, comparable over so prolonged a period, differ slightly from the batch fatality rates averaged for similar periods (Table I), they both'tell the same tale.

TABLE III.—RATIO OF ANNUAL TOTALS OF DEATHS TO CASES FOR ENGLAND AND WALES AND LONDON AND GREAT TOWNS, MEAN ANNUAL BATCH FATALITY RATES, LONDON AND GREAT TOWNS AND WHOOPING COUGH MULTIPLES OF CORRESPONDING MEASLES RATES.

		London and Great Towns			London and Great Towns			England and Wales		
Years		C.F.R. Annual totals Deaths per 1,000 cases	Wh. C. multiples of measles C.F.R.	2 yrs. mean	B.F.R.	Wh. C. multiples	2 yrs. mean	C.F.R. Annual totals Deaths per 1,000 cases	Wh. C. multiples	2 yrs. mean
1940	Whooping cough	13·3	5·1	4·8	16·9	5·8	5·4	12·6	6	5·4
	Measles	2·6			2·9			2·1		
1941	,,	15·4	4·5		14·7	4·9		13·7	4·9	
	,,	3·4			3·0			2·8		
1942	,,	13·6	8·0	6·4	13·6	7·2	6·5	12·1	7·6	6·6
	,,	1·7			1·9			1·6		
1943	,,	12·3	4·7		12·5	5·7		11·6	5·8	
	,,	2·5			2·2			2·0		
1944	,,	12·3	7·2	6·8	12·5	6·9	6·2	11·2	7·5	7·2
	,,	1·7			1·8			1·5		
1945	,,	11·5	6·4		11·1	5·9		11·0	6·9	
	,,	1·8			1·9			1·6		

It is to be noted, however, that the high batch fatality rates of whooping cough in the early months of 1940, never afterwards approached, are, relatively to subsequent rates, probably exaggerated. Statutory notification of whooping cough and measles, recently imposed, was almost certainly less complete in the earlier months of its operation than later. There is, in the case of whooping cough, an additional lag due to the fact that notification is usually delayed until late when the whoop has developed. The diminution due to this delay is, when notification has got into its stride, in some measure, compensated by the legacy of preceding similarly-acting deferment. It is probably for this reason also that the annual averages of the monthly batch fatality rates give for the year 1940 a rate very considerably in excess of the case fatality calculated from the smoothing annual totals of cases and deaths. The year 1940 is the only one in the six years' series, in which there is a difference in the annual rates calculated by these respective methods, so great that it would show to the first place of decimals in rate, as commonly expressed, of deaths per 100 cases.

Measles fatality, it will be seen from the tables, is falling more rapidly than the case fatality of whooping cough both in the Great Towns, and in England and Wales. This retardation, relative to that of measles in the decline of whooping cough fatality, is the more clearly seen if, in the successive two-yearly periods in which the measles epidemics respectively run their course, the ratio of the fatality rates of the two diseases in the relative years is compared.

Case fatality in hospitals—M.A.B. and L.C.C.—The most reliable figures of case fatality in the pre-notification period come from hospitals where the numbers of cases and deaths are known precisely (Table IV). Unfortunately, however, owing to the selective character of the cases, these, in many respects, are not comparable with figures which would have been yielded by corresponding cases and deaths among the general population.

TABLE IV.—CASE FATALITY IN M.A.B. AND L.C.C. HOSPITALS.

Years	Whooping cough case fatality rate per 1,000	Measles case fatality rate per 1,000
1910–14 ..	108	116
1915–19 ..	123	109
1920–24 ..	100	90
1925–29 ..	130	69
1930–34 ..	91	52
1935–39 ..	57	28
1940–44 ..	34	6·4

Figures by courtesy of Sir Allen Daley.

Measles fatality has declined in hospital more rapidly than whooping cough though both continue to fall; and right up to the present time, as shown also by batch fatality rates, the reduction in case fatality is for both a striking and even an astonishing feature.

Persistent as for many years, within the limited field of observation possible, has been the decline in case fatality, notification revealed, at least in the case of measles, a fall which must be regarded as abrupt. This I have already discussed (*J. R. statist. Soc.*, 1945, **108**, Pts. 3 and 4). With regard to whooping cough, in a personal communication from Sir Allen Daley he says “that the sharp fall in case fatality in 1939 was shared by the whole community” and in support of this says, “Some comparison of the incidence of whooping cough in 1938 and 1939 can be made from the reports of cases noted by head teachers at schools, though these reports ceased to be complete after the middle of 1939, owing to the dispersal of school children. For the first six months of each year the figures are 2,025 in 1938 and 7,125 in 1939. Thus in the first half of 1939 the incidence was three times as heavy as in the same period of 1938. Deaths in the first half of 1939 were 91 compared with 72 in the first half of 1938, whereas the expected figure on 1938 case mortality would be in the region of 250”. Case fatality on the above figures shows a fall of from 35 to 13 per 1,000 and is thus quite as striking in whooping cough as in measles.

In measles there seems good reason to believe that the decline in case fatality is in considerable measure due to changes in age-incidence, and it is possible that whooping cough fatality, which has behaved in like manner may be similarly accounted for. Dispersal of children which was so marked a feature of 1939, diffusing infection of measles, of whooping cough and other diseases among persons normally less in contact with infection and of higher age-periods than school children, hitherto the most intensively exposed, may well account for the abrupt fall in case mortality in both diseases. Stocks has shown that the dispersal of children had the effect in certain regions of keeping down the whooping cough rate in the evacuation towns, but in the reception areas evacuees with a higher incidence were mingling with an adult population less protected than that from which the children had been evacuated. It is not the whole story. There are other factors persistently modifying the course and character of these familiar epidemic diseases, but the dispersal of juveniles both in the evacuation and in the reception areas at the outbreak of war was calculated to produce just such striking results as we have observed.

Age distribution of cases.—So far we have considered the behaviour of case fatality at all ages. It has for long been established that both diseases are much more fatal in early than in later life and the case distribution according to age becomes important on this account, since case fatality will be higher the greater the proportion attacked at the more vital age-periods. I have been able to cull a random sample of some 15,000 cases of whooping cough and 33,000 cases of measles from recent annual reports of those relatively few Medical Officers of Health who have set out their analyses.

TABLE V.—AGE DISTRIBUTION OF APPROXIMATELY 15,000 CASES OF WHOOPING COUGH AND 33,000 CASES OF MEASLES.

(*a*) In County and Municipal Boroughs and Urban Districts.
(*b*) In Rural Districts.

	Whooping cough				Measles			
	All ages	0–1	0–5	5 and over	All ages	0–1	0–5	5 and over
(*a*) Urban	13,238	1,694	9,320	3,918	28,970	1,472	15,747	13,223
Percentage All ages = 100		12·8	70·4	29·6		5·1	54·3	45·6
(*b*) Rural	1,593	137	931	662	4,090	116	1,632	2,458
Percentage All ages = 100		8·6	58·4	41·6		2·6	38·9	60·1
Totals (*a*) and (*b*)	14,831	1,831	10,251	4,580	33,060	1,588	17,379	15,681
Percentage All ages = 100		12·3	68·8	30·2		4·8	52·6	47·4
Comparative sample Measles taken earlier in notification period.					25,628	1,087 4·2	13,495 52·6	12,133 47·4
England and Wales 1944*		10·8	64·0	36·0		3·9	47·7	52·3
,, ,, ,, 1945†		10·7	66·7	33·4		4·3	52·7	47·0
,, ,, ,, 1946†		9·4	66·4	33·5		4·6	53·8	46·8

*Figures in Ministry of Health C.M.O. Rep. on the State of the Public Health, 1939–45.
†Figures in Registrar-General's Quarterly Returns.

The figures relate to cases of whooping cough and measles taken at random throughout England and Wales. In place and period their respective occurrence was identical. Those relating to Rural Districts are small but sufficient, I think, to reflect with approximate truth the differences between urban and rural incidence of these diseases. I have added to the table the figures of another and quite different random sample I had previously recorded (*J. R. statist. Soc.*, 1945, **108**, Pts. 3 and 4) of measles notifications similarly distributed. The almost identical proportions of distribution in these different samples is presumptive that they are characteristic. I think the figures demonstrate some important features in the recent behaviour of the two diseases.

(*a*) Whooping cough attacks infants in much higher proportion than does measles and both have higher incidence upon urban than upon rural infants.

(*b*) The proportion of persons attacked over 5 years of age is considerably higher in measles than in whooping cough and is much higher in the former than, before notification came into operation, one would have expected. Again the proportion is higher in rural districts than among urban populations.

During the first 6 months of life infants are little susceptible to measles but no such protection is afforded against whooping cough, in fact susceptibility to this disease in early childhood appears to be exceptionally emphasized. In the 0 to 5 age-group children are attacked in very much greater proportion in towns than in rural districts, as might be expected. Since liability to attack when exposure occurs must, in children not already protected by previous attack, be pretty much the same in both diseases and since opportunity of exposure must, in the more prevalent measles, be greater, it is difficult to understand why early childhood should be selected to bear the brunt of whooping cough and even though no congenital immunity in the early months of infancy safeguards the baby from this disease its native seclusion should afford sufficient protection save when other members of the family become affected. I have also included in the table the ratios of age-incidence of measles and whooping cough for England and Wales. It will be seen that the proportions to those at all ages, at the respective age-periods given in the random sample, are in agreement with those shown by the much more comprehensive figures, which, in fact, give ratios intermediate between those of urban and rural districts, not distinguished in the figures for England and Wales.

Sex incidence.—The ratios of male to female cases in all age-groups in 1944–46 are distinctive for the two diseases, and show very little variation with age except in the over 15 age-group in which the numbers of cases are small.

Unfortunately corresponding distribution of deaths is insufficiently available to enable case fatality at age-periods to be calculated on a scale that is adequate. London hospital figures (M.A.B. and later L.C.C.) show how at each age-period case fatality has been declining during the last thirty years.

TABLE VI.

	Whooping Cough				Measles		
1910·14	Cases	Deaths	Case fatality per 100	1910–14	Cases	Deaths	Case fatality per 100
0–1	675	165	24·4				
0–5	4,113	501	12·2				
5 and over ..	646	14	2·2				
All ages ..	4,759	515	10·8	All ages	11,925	1,388	11·6
1935–38				1935–39			
0–1	1,628	362	22·2				
0–5	8,194	636	7·8				
5 and over ..	1,217	21	1·7				
All ages ..	9,411	657	7·0	All ages	25,954	739	2·8
1939–40				1940–44			
0–1	871	77	8·8				
0–5	3,867	115	3·0				
5 and over ..	540	3	0·5				
All ages ..	4,407	118	2·7	All ages	18,286	118	0·6

Measles fatality has declined in hospital more rapidly than whooping cough though both continue to fall; and right up to the present time, as shown also by batch fatality rates, the reduction in case fatality is for both a striking and even an astonishing feature.

Persistent as for many years, within the limited field of observation possible, has been the decline in case fatality, notification revealed, at least in the case of measles, a fall which must be regarded as abrupt. This I have already discussed (*J. R. statist. Soc.*, 1945, 108, Pts. 3 and 4). With regard to whooping cough, in a personal communication from Sir Allen Daley he says "that the sharp fall in case fatality in 1939 was shared by the whole community" and in support of this says, "Some comparison of the incidence of whooping cough in 1938 and 1939 can be made from the reports of cases noted by head teachers at schools, though these reports ceased to be complete after the middle of 1939, owing to the dispersal of school children. For the first six months of each year the figures are 2,025 in 1938 and 7,125 in 1939. Thus in the first half of 1939 the incidence was three times as heavy as in the same period of 1938. Deaths in the first half of 1939 were 91 compared with 72 in the first half of 1938, whereas the expected figure on 1938 case mortality would be in the region of 250". Case fatality on the above figures shows a fall of from 35 to 13 per 1,000 and is thus quite as striking in whooping cough as in measles.

In measles there seems good reason to believe that the decline in case fatality is in considerable measure due to changes in age-incidence, and it is possible that whooping cough fatality, which has behaved in like manner may be similarly accounted for. Dispersal of children which was so marked a feature of 1939, diffusing infection of measles, of whooping cough and other diseases among persons normally less in contact with infection and of higher age-periods than school children, hitherto the most intensively exposed, may well account for the abrupt fall in case mortality in both diseases. Stocks has shown that the dispersal of children had the effect in certain regions of keeping down the whooping cough rate in the evacuation towns, but in the reception areas evacuees with a higher incidence were mingling with an adult population less protected than that from which the children had been evacuated. It is not the whole story. There are other factors persistently modifying the course and character of these familiar epidemic diseases, but the dispersal of juveniles both in the evacuation and in the reception areas at the outbreak of war was calculated to produce just such striking results as we have observed.

Age distribution of cases.—So far we have considered the behaviour of case fatality at all ages. It has for long been established that both diseases are much more fatal in early than in later life and the case distribution according to age becomes important on this account, since case fatality will be higher the greater the proportion attacked at the more vital age-periods. I have been able to cull a random sample of some 15,000 cases of whooping cough and 33,000 cases of measles from recent annual reports of those relatively few Medical Officers of Health who have set out their analyses.

TABLE V.—AGE DISTRIBUTION OF APPROXIMATELY 15,000 CASES OF WHOOPING COUGH AND 33,000 CASES OF MEASLES.

(*a*) In County and Municipal Boroughs and Urban Districts.
(*b*) In Rural Districts.

	Whooping cough				Measles			
	All ages	0–1	0–5	5 and over	All ages	0–1	0–5	5 and over
(*a*) Urban	13,238	1,694	9,320	3,918	28,970	1,472	15,747	13,223
Percentage All ages = 100		12·8	70·4	29·6		5·1	54·3	45·6
(*b*) Rural	1,593	137	931	662	4,090	116	1,632	2,458
Percentage All ages = 100		8·6	58·4	41·6		2·6	38·9	60·1
Totals (*a*) and (*b*)	14,831	1,831	10,251	4,580	33,060	1,588	17,379	15,681
Percentage All ages = 100		12·3	68·8	30·2		4·8	52·6	47·4
Comparative sample Measles taken earlier in notification period.					25,628	1,087 4·2	13,495 52·6	12,133 47·4
England and Wales 1944*		10·8	64·0	36·0		3·9	47·7	52·3
" " " 1945†		10·7	66·7	33·4		4·3	52·7	47·0
" " " 1946†		9·4	66·4	33·5		4·6	53·8	46·8

*Figures in Ministry of Health C.M.O. Rep. on the State of the Public Health, 1939–45.
†Figures in Registrar-General's Quarterly Returns.

activity maintaining at lower levels an endemic continuum. To this latter type both whooping cough and measles belong and in this respect differ from intermittent invaders such as, in Europe, are cholera, plague, smallpox and other occasional visitors. A succession of Registrar-Generals, and their medical advisers, have given voluminous, invaluable records, mostly in terms of deaths, of the courses and other epidemic features of measles and whooping cough in England and Wales. Six years of statutory notification of measles and whooping cough on an inclusive basis throughout England and Wales have placed for the first time at the disposal of investigators a store of facts which enables case distribution to be shown on a scale not only not hitherto available but on one sufficiently comprehensive to give a presumption of the distribution being characteristic. The six years' notification records relate to a period—war and post-war years—in which conditions affecting prevalence have been far from normal. It is possible, therefore, that we are dealing with somewhat atypical epidemic occurrences and so it would be wrong to assert of observed fact anything but its current truth. Nevertheless the broad features at least of measles epidemics appear not to have altered. I have made (*see Monthly Bull. Min. Hlth.*, April 1946) a comparison of graphs showing the composite weekly means of notified cases of the three epidemics of measles, London and the Great Towns 1940–1945, and the composite weekly means constructed from deaths and school-notified cases of three epidemics, London 1908–1913. As may be seen by reference to the graphs (reproduced with the article) the respective epidemics follow a common course in which resemblance in all outstanding features is very striking. Measles more than whooping cough exhibits repetitive epidemic features, though it is possible that in the case of whooping cough the gamut of the notification period is insufficient for the development of periodicity analogues, if, in fact, they occur.

Differences in the epidemic course, shown respectively by deaths and cases.—Comparison of corresponding graphs of cases and of deaths similarly plotted bears out what would be expected from consideration of the differences in seasonal case fatality. Taking the extreme range in the case fatality exhibited, that between the end of August 1945 and the end of January 1946, the batch fatality rates were found to vary from 0·2 to 7·6 per thousand. "A given number of deaths would at the lower rate yield a total of cases 38 times the number calculated at the higher rate" (*Monthly Bull. Min. of Hlth.*, May 1946). With a mean number of weekly deaths of 15 the calculated number of cases per week would, with this range of case fatality, vary from 2,000 to 75,000 and this potentially wide range of error, where a flat rate of fatality had to be assumed, inevitably must greatly disturb seasonal distribution when deaths are translated into calculated cases. The monthly distribution respectively of cases and of deaths each as a proportion of their respective six years' means does not, however, as may be seen from the diagrams, so greatly vary the main epidemic features that they are not in each series clearly exhibited. Taken separately either for the two-yearly periods within which each of the three epidemics ran its course (fig. 2, *a*, *b*, and *c*) or, for the average figures (fig. 2, *d*), seen in the six-yearly composite graphs, these features, characteristic of measles, are easily perceptible whether the graphs be of deaths or of cases. Alike, in contemporary and in successive epidemics, the minor and the major phases, the summer maximum of the minor phase, the autumnal notch, the re-commencing ascent in September–October, the maximum peak of the second year and thereafter the rapid fall and maintenance for several months in late autumn and early winter of a low, practically uniform level of sub-epidemic or endemic prevalence are common to all graphs. Nevertheless, differences and distortions of proportionate prevalence are shown in the death graphs as compared with those of actual cases. In the winter months, except when anomalous low fatality occurs, the graphs of deaths are relatively much higher and in the months of low case fatality proportionately lower than the graphs of cases. This has the apparent effect in the deaths graphs of greatly reducing the volume of the minor phases which attain their maxima in the summer months of low fatality, when cases are represented by few deaths, and of lengthening the peaks of the major phases which coincide with months of high case fatality when a given number of cases are represented relatively by more deaths. This, of course, is what we should expect and without more than indicating the kind and magnitude of these differences we may pass to consideration more fully of the graphs in which they are displayed.

The graphs.—During the six completed years within which statutory notification has operated—1940–45—all the epidemics of measles have bestridden the calendar divisions between years in each of all three successive biennial periods. The complete course of an epidemic, therefore, could be exhibited only in a span which included parts at least of two successive years. It was found that the beginning of the first year of each such span coincided approximately with a commencing epidemic rise, immediately following a sub-epidemic level sustained during several preceding months. Commencing at the beginning of one year each epidemic attained maximum incidence in the next and, some months before the end of the year, subsided, to just such a level as that from which it sprang.

TABLE VII.—ENGLAND AND WALES.

Whooping Cough and Measles Notifications. Proportional Age and Sex Distribution on Totals of 1944, 1945 and Six Months of 1946

	All ages	0–1	1–3	3–5	5–10	10–15	15 and over
				Whooping Cough			
Sex ratios 100 F/M	112	101	108	112	112	120	331
Proportion all ages =	100	M 11·1 F. 10·1	28·3 27·5	27·5 27·6	30·1 30·8	2·4 2·6	0·8 2·3
				Measles			
Sex ratios 100 F/M	100	97	94	97	99	110	203
Proportion all ages =	100	M 4·3 F 3·9	22·6 21·2	26·1 25·2	40·5 40·2	5·0 5·5	2·8 4·2

As already pointed out hospital figures in many respects are not comparable with those relating to the general population. For well-known reasons they are higher, but there can be little doubt that they reflect at the times to which they relate, and in their respective age proportions, analogues in rates which differ from those of the general population principally in their order.

One fact of great interest remains unaffected by recent data. The established high fatality of both diseases in the first two years of life, greater in the case of whooping cough and especially in infants, is perhaps, from the point of view of preventive practice, the most significant feature in their behaviour. That whooping cough is more deadly even than measles in the first year of life is in part due to the fact that while most infants have a respite from measles during the first six months no such congenital immunity is extended to whooping cough. Approximately whooping cough has twice the opportunity in time to claim its fatalities in the first twelve months of childhood. There is for the young infant no compensatory protection from whooping cough which the sex of the mother predisposes her to contract and—whether on this account or not—in higher proportion than the male sex to die of the disease. Immunization of the mother by actual attack appears not to be as in measles congenitally transmissible even for a brief period. Moreover as Stocks has pointed out (*J. Hyg.*, 1932, 32) "the loss of acquired latent immunity is more rapid than in measles and little or none remains after a year". In measles apparently it lasts for two or three years. Not only the acquired latent variety but the active immunity conferred by attack appears subject to the same rule. I myself have been the victim of three attacks of whooping cough at intervals approximately of twenty-five and forty-five years respectively between the first and second and the second and third occurrences. This is doubtless very exceptional though I have known of a number of adults who have suffered attack notwithstanding that in childhood they had undergone a primary salting. In measles second attacks are rare; in whooping cough acquired immunity is permanent to a lesser degree than the high protection extended usually for life in the case of measles.

Immunities, congenital, latent or active following fully developed attack are co-determinants of epidemic developments and endings. With apparently universal susceptibility to whooping cough from birth, and to measles after six months of congenital protection, these diseases are the commonest and most widespread of the scourges of childhood. Deferred to the ages and seasons of low fatality, therapeutically cared for on a scale co-extensive with that of diffusion, there is, as a growing trend reflected in lower and declining fatality demonstrates, a prospect of protection to the community at a sacrifice which is but a fraction of that hitherto claimed. It is neither practicable nor desirable wholly to prevent diffusion throughout the community of ever-present infections to which all, until immunity has been acquired, are highly susceptible. It looks as though the time may not be distant when such immunity may be conferred by specifically directed measures. Till that is possible preventive efforts should consist, not in futile attempts by time-honoured but inappropriate means aimed at limiting immediate diffusion from cases, for this purpose belatedly coming to knowledge, but rather in noting the natural behaviour of these diseases by appropriate social and other administrative adjustments, so arranging that as far as possible the inevitable personal attack befalls when it is least dangerous to the patient.

EPIDEMIC BEHAVIOUR

The epidemiologist is concerned with the incidence of communicable diseases as seen affecting masses of the population. Their prevalence may be sporadic, epidemic, endemic or of a mixed description as when, between epidemic exacerbations there is a sub-epidemic

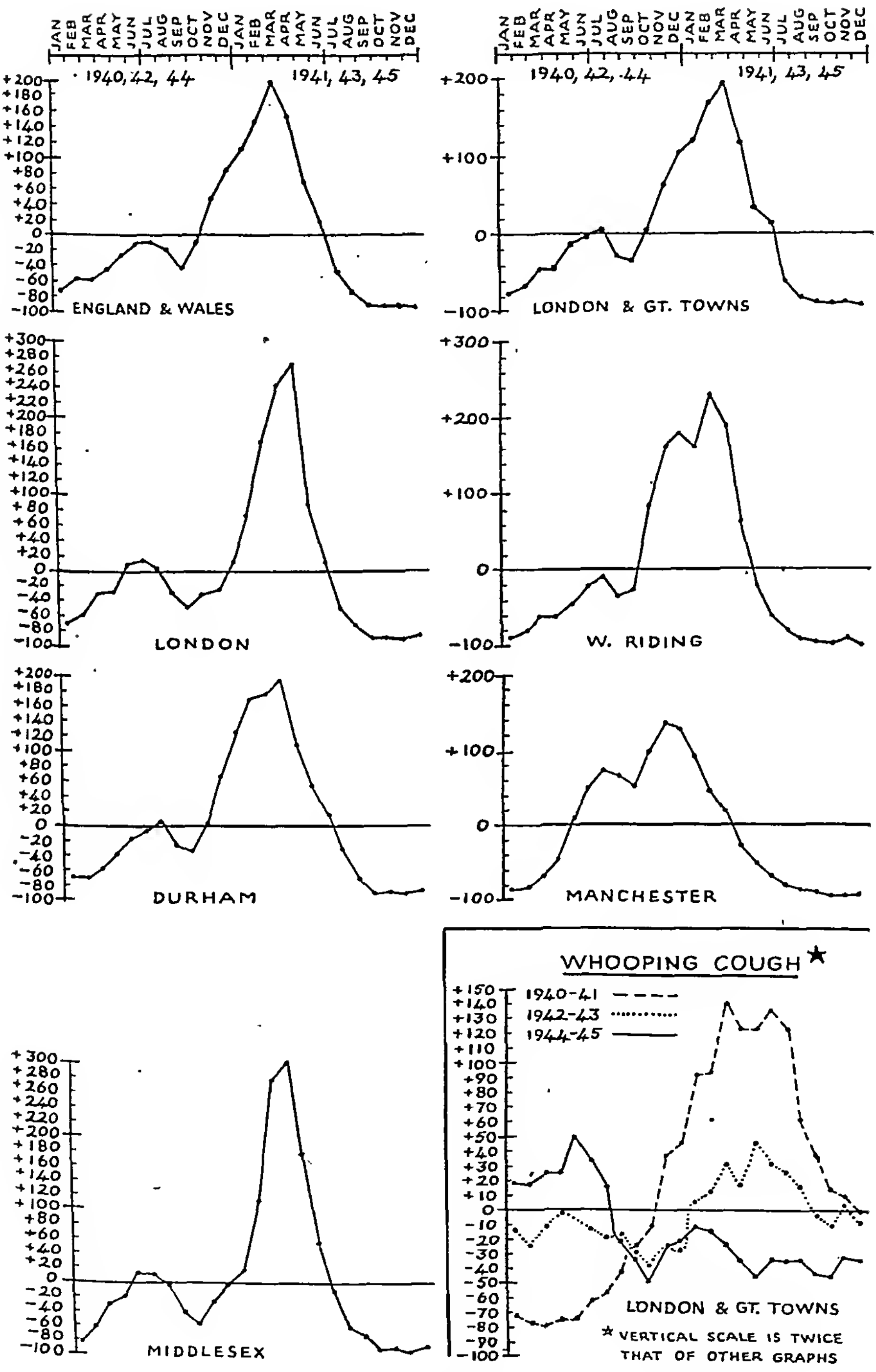


Fig. 3

MEASLES. Composite of Three Epidemics. Years 1940-1945.

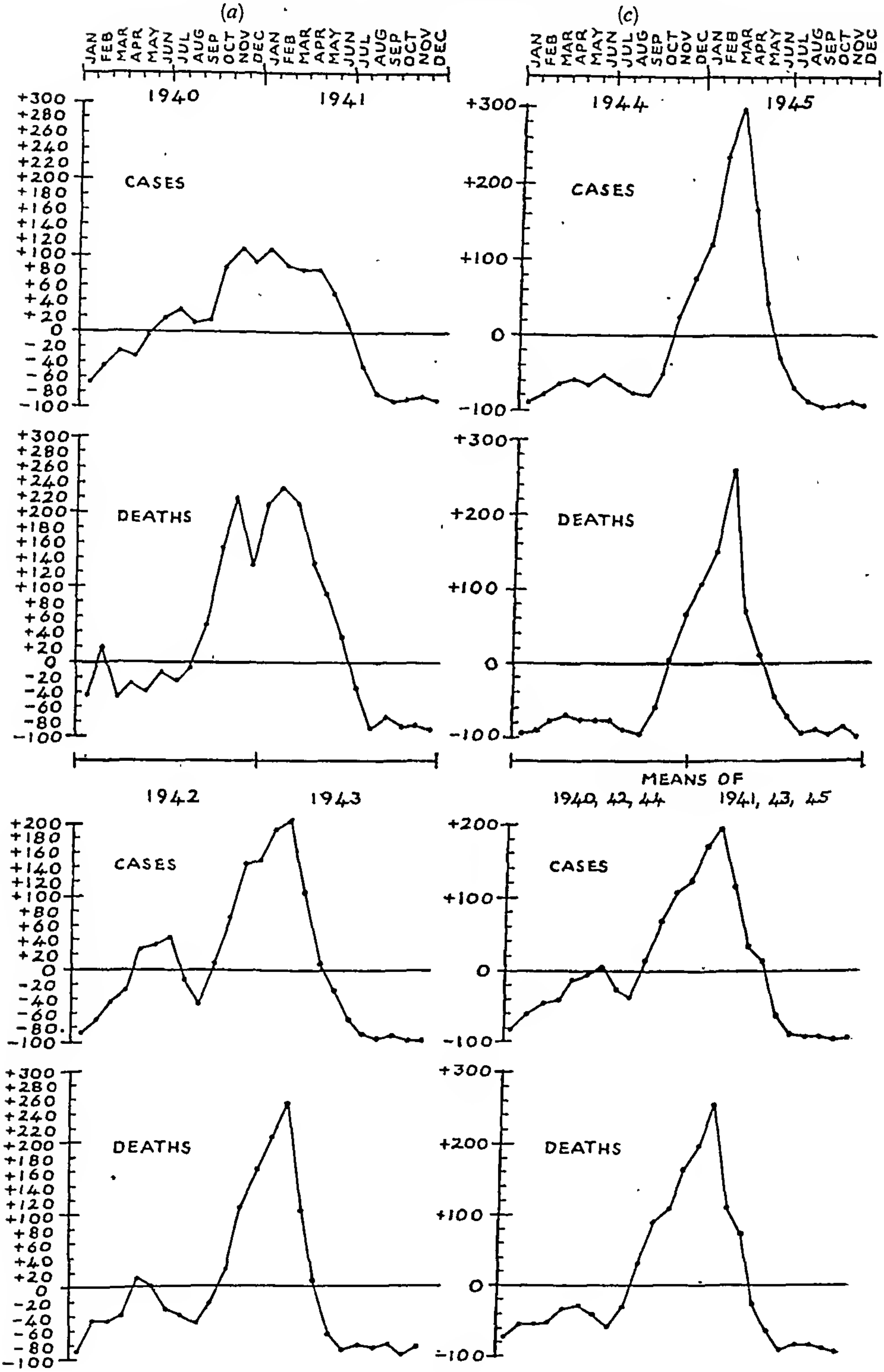


Fig. 2

(*b*) (*d*)

MEASLES. LONDON AND GREAT TOWNS. Respective graphs of cases and deaths.

that month was the break, not in the ascent but in its steepness previously uninterrupted from April to July. In the epidemic, 1942–43 (fig. 4*c*), again in Manchester, which acts to-day as England may to-morrow, the customary minor phase in May attained a maximum higher than that reached in the December of what usually is the major phase. That in London again the minor phase of the epidemic, 1940–41 (fig. 4*b*), was atypical, almost lacking in fact, was due no doubt as were other atypical developments of the epidemic to the very extensive evacuation of children which then characterized the metropolis.

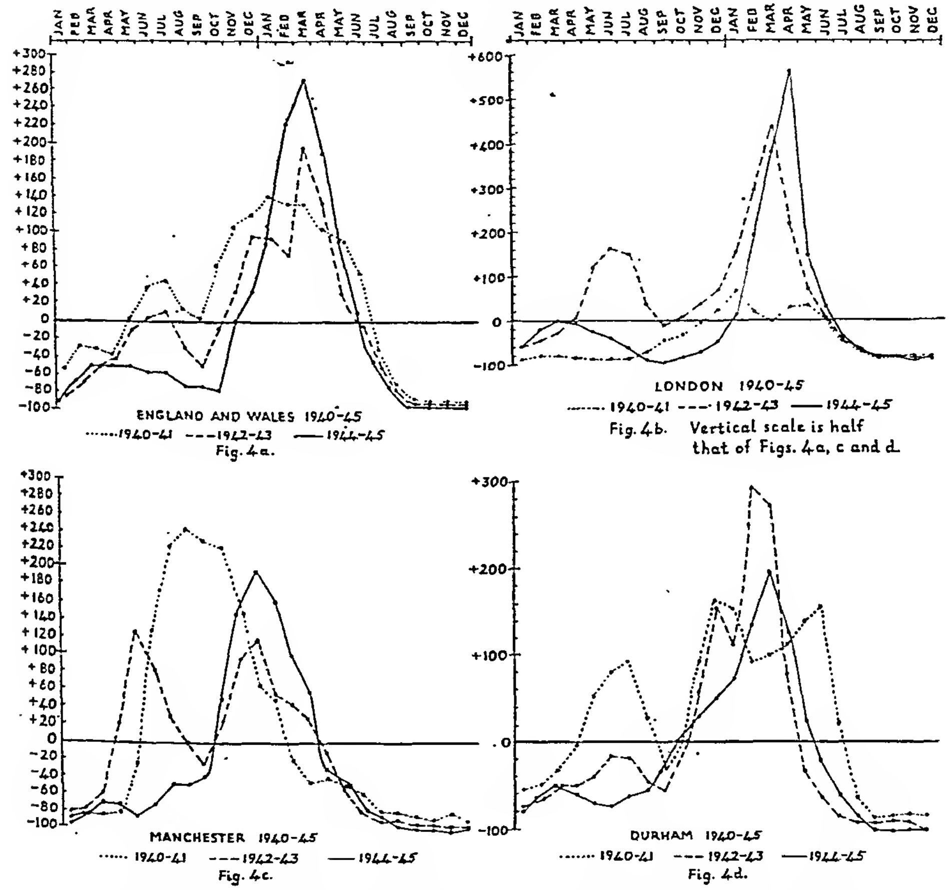


Fig. 4a. Fig. 4b. Fig. 4c. Fig. 4d.

FIG. 4 *a*, *b*, *c* and *d*.—MEASLES. Superimposed biennial distribution—6 years.

It is to be noted that in none of the instances, in which these aberrant forms were presented, did the composite graph of the other two of the three epidemics depart from the type to which the others in the six years' records of the prevalence conform. Further, the chronological order of development in the aberrant types may vary and in their maximal incidence revert exceptionally to a season noted in the past as common and yet in general feature resemble what is claimed as the unmistakable type of current measles. It is as though, if one may import an animism, that when conformity to type was thwarted, a corrective reaction marked subsequent activities.

The sub-epidemic phase.—There is one other feature of the graphs of measles to which attention should be directed, a negative one, but different from the others in that it does not vary and so is common to all the graphs. In the September of the second year of epidemicity, incidence has fallen rapidly as a rule, to a level from which on the scale on which the graphs are drawn there is scarcely a perceptible change for the rest of the year. The monthly averages, ranging within the low sub-epidemic limits of between 80% and 90% below the mean, are represented from September to December by what is virtually a straight line. The earlier September level, following the minor phase in the first year of epidemicity is also, almost with the same invariability, the lowest, after the initial stage and before that

It followed, therefore, that within each of three successive two-yearly spans into which the six years' notification period was divisible there were comprised an epidemic and a succeeding inter-epidemic period, each virtually complete. And this is so, as illustrated in the graphs whether the notifications for England and Wales, London and the Great Towns, counties such as Middlesex, the West Riding, Durham, Lancashire and Cheshire or great cities such as London, Manchester and Liverpool were severally subjected to such an analysis. While the course of a measles epidemic is thus displayed within a two-years' span, its actual duration falls well within that time. In none of the graphs does it exceed twenty months from the perceptible rise in January of the first year of epidemicity to its fall to sub-epidemic levels in August of the year following. And, indeed, there is little departure from this rule. It may, of course, be argued that within this span we are dealing, as has often been taken to be the case, not with a single, but with two epidemics. I think that the graphs render this view untenable, but this will be the better appreciated when we have considered more fully the features disclosed.

Epidemic beginnings.—The commencing point of each epidemic coincides approximately, as has just been said, with the beginning of the year of its initial development. But in the first, 1940–41, of the three series of epidemics which six years' notification has disclosed, already at the beginning of January a rise above sub-epidemic levels has been attained, but to a height which, if the curve be retrojected[1], places the start only a few weeks in advance of the commencing year. In the January, two years later, the level is a little lower and lower still, in fact barely perceptible, in the first month of the third two-yearly span. This means that each epidemic started just a little later in each succeeding epidemic period. This is not uniformly true of all the graphs, but is readily seen in those both of England and Wales (fig. 4*a*) and London and the Great Towns (fig. 2). The time of commencement does, presumably, make a difference to the subsequent development of an epidemic; the older it is, the sooner, *ceteris paribus*, its course is likely to be unfolded and completed. A procession of commencing dates and later developmental features in serial epidemics, should they, by more prolonged observations, be established, would greatly modify recurrent periodicities if they are, as they may be, chronologically, rather than seasonally, determined.

In the Statistical Review of the Registrar-General, 1921–25, attention is called to some notable changes in the seasonal curves of deaths from measles in which during a number of years "the gap between winter and spring peaks had filled up completely for London and almost completely for England and Wales. . . . The stages of this change for London are shown in the weekly returns from which it appears that in 1891–95 the February depression was pronounced, but that by 1911–15 its last traces had disappeared". It is the fact of these changes in peaks and gaps at the seasons named to which I wish to call attention. Neither the winter peak nor the February depression between it and the still surviving March maximum are generally to be recognized in the graphs of notifications with which we are dealing, though a cleft in the February of the major phase of the cases graph—England and Wales, 1942–43 epidemic (fig. 4*a*), and a similar depression corresponding in phase in the 1940–41 Durham epidemic (fig. 4*d*)—suggests that in these atavistic vagaries there may be a recent representative of the earlier notch. If over long periods certain valleys may be exalted and certain peaks laid low, the process, conceivably, may be one with a procession, a recession or an oscillation in the season of beginning epidemicity.

Epidemic phases.—The course of measles, graphed as above described, shows within each two-year span a minor and a major phase of epidemicity, separated by what I have called the autumnal notch and terminated by a spell of continuous sub-epidemic activity. Conformity to type is always a variable quantity and it is in accord with the proclivities of the typical that, in particular instances, wide departures may be shown amounting at times to total absence of a specific characteristic feature. In measles, epidemic types are no exception in their possession of aberrant members. For instance, the minor phase in the West Riding epidemic, 1944–45 (fig. 5, *see* p. 386), was wholly lacking and the epidemic, commencing in October, normally the eighth month of epidemic prevalence, continued thereafter in general conformity to the customary course, attaining its maximum in March—unlike its two predecessors with erratic maxima respectively in November and December—and completing its subsidence by August. But, lacking the minor phase, the epidemic is shortened to a single pinnacle of unwonted altitude, in this resembling the London epidemic of the same period where a minor phase, not lacking, but aborted, was followed by a similar pinnacle, the highest of any in the epidemics examined. Again in Manchester in the epidemic, 1940–41 (fig. 4*c*), the minor phase commencing late was merged completely with that of the major, the dividing autumnal notch being wholly absent and the customary low incidence of August replaced by a maximum peak in which the only tribute to the usual depression of

[1] Notification had come into operation only shortly before this and could not yet be said to have got into its stride.

not less than the striking, occasionally violent, outbursts which from time to time dominate attention.

In measles, a just-continuing persistence, in whooping cough, an apparently erratic sub-epidemicity, are the reservoirs from which spring the spectacular outbreaks apt to monopolize observation to the neglect of the no less important, though less obtrusive, modes of prevalence.

Not apparently seasonally determined, though, as seen in the measles graphs, regularly from September to December, in alternate years, seasonally exhibited, they are an enduring source from which, when circumstances favour, are started the rising prevalences that culminate in epidemics. Whooping cough shows little proclivity to regular periodicity either in its general or inter-epidemic features and measles, in this phase of prolonged quiescence, is in contrast with its seasonal behaviour in alternate years, when, in the same months, following the autumnal notch, there is, normally, a rapid and continuing rise to epidemic heights.

It cannot be that identical months exhibit seasonal influence in so diverse a manner, and alternating seasonal exhibition of these opposed phases of incidence can mean only that they are determined otherwise than by seasonal influences. But the significance of the continuing lowered incidence between epidemics of measles and whooping cough is that in this endemic diffusion the train is laid so that never are the potentially explosive foci arising with each cessation of epidemicity far removed from the smouldering embers so readily converted to igniting sparks.

In neither of these affections is there reason to believe that the *materies morbi* have an independent, extra-corporeal career. Proliferation of the virus is almost certainly synonymous with microbial cytogenesis within the bodies of its increasing victims. When Brownlee (*Proc. R. Soc. Med.*, 1919, 12, 77) speaking of measles announced that "An epidemic is due chiefly to the properties of the organism causing it and that the periodicity of epidemics which occur at regular intervals depends for the most part on the life-history of the organism" he may have been prepared to accept the proposition that there was no reason to believe that at any time in its life-history was the measles organism saprophytic, and, if this be so, the significance of endemic continuity needs no emphasis. And we may, in passing, inquire as to whether periodicities or other features of epidemics can properly be spoken of as determined mainly by the properties of the organism causing them or, conversely, as due to co-ordinate qualities, the necessary proportionate correlative vulnerability in the populations threatened. The antithesis is false, for apparent variations in virulence of the organism are meaningless save in terms of implicit constants of susceptibility or alternatively of corresponding changes in immunity of infected persons. Infective, susceptible—obverse aspects of the same phenomenon, how shall we say of either that it is the chief; upon which of two reciprocals, for the most part, depends a result to which both are indispensable? The cause of an epidemic is never wholly the diffusion of organisms of constant or changing pathogenicity, never alone an accumulation of relatively susceptible persons, but always the two together. Without one and the other you cannot have the resultant cases.

CONCLUSION

Though whooping cough and measles are kindred epidemiologically, in many of their features, clinically, they are most dissimilar. Measles, one of the exanthemata akin to smallpox with which its affinities are so close that for long the diseases remained undistinguished one from the other, is in a category removed from the non-eruptive disease that has taken its description from its mastering, paroxysmal cough. Initially more catarrhal, more sharply febrile, brief in its duration if uncomplicated, measles spends itself selectively in inflammatory epithelial lesions.

Whooping cough, more insidious in its onset, prolonged in its growing distress, less prone primarily to involve the tissues in extensive inflammatory changes, is almost devoid of pathological histology. Increasingly, as it matures, its symptomatology is that of neural disturbance. The paroxysmal neurosis dominates, sharing in wider, less terrorizing functional disturbances unaccompanied by perceptible structural neural changes, the selective toxins of whooping cough in this differing from those of diphtheria which so often result in late organic paralyses.

That two diseases, clinically so unlike, each presenting fundamental contrasts of behaviour, measles notably in its biennial cycles of recurrence, whooping cough in this and other respects in erratic disunity, should yet otherwise exhibit so close an epidemiological concert and together have travelled so far toward a common destiny, is an unexpected result from so strangely assorted a yoking. Preventive technique must aim not, as in such epidemic diseases for instance as typhus and typhoid, at attempting to prevent their prevalence, but reached with the final fall, in the whole course of epidemic prevalence, but unlike the fall in the September following, it is immediately, in October, followed by resumption of the ascent which had been interrupted by the autumnal notch. This difference in the behaviour of measles at the conclusion respectively of the minor and the major phases is, perhaps, as convincing an evidence that they are phases and not alternating minor and major epidemics, as any presented by the graphs. If the phases be conceded features of a single epidemic, biennial periodicity remains a suitable description of epidemic recurrences so related, even more appropriate because more embracing than when applied only to biennially recurring peaks separated by a void. On the other hand, if the minor phase be regarded as in no sense one of epidemic prevalence, either of one or of separate epidemics, it becomes a nondescript incidence, somehow relegated to sub-epidemic levels to which discernibly it rarely descends. Should one be able to rest in such a contradiction he would be free to regard the surviving major incidence exclusively as an epidemic, relatively short-lived and alternating with a year of non-epidemic mixed flat and undulating prevalence. This, usually, is what is meant by biennial periodicity. Yet again the minor phases as such may cease and, if enlarged and separated by definite sub-epidemicity from what follows, be regarded justly as completed epidemics. In that case, of course, biennial periodicity disappears and is replaced by annual recurrences. But in the graphs of incidence of recent years there is seen to be comprised within a single span of four-and-twenty months the proportioned phases not alone of epidemic prevalence but also of the low levels of intercurrent sub-epidemicity. Thus seen, periodicity ceases to be a biennial recurrence of punctual maxima and becomes a periodic repetition of like prevalences each in its due season, once within two years. Ultimately the present forms of measles prevalences may be shown to be, as presented, impermanent; they may prove to be transitional stages to or from such a form of biennial periodicity as, hitherto, for the most part, it has been conceived. If the movement be towards a single peaked form recurring biennially, the minor phase together with the autumnal notch will each disappear and be reduced to levels uniformly sub-epidemic; if away from such a biennially periodic type and towards that of annual recurrence, the minor phase will expand, the autumnal notch deepen, and there may thus emerge annually recurring epidemics separated by sub-epidemic phases, long and short in alternate years. Exceptional forms of prevalence among those examined may be said to be illustrative of either trend.

Epidemic behaviour of whooping cough.—So much for the serial distribution of measles: what of whooping cough? Similarly treated to exhibit features of prevalence, the graphs are not helpful. So far from conformity to design being established, type has not even emerged. In his account of the epidemiology of whooping cough, Professor Bradford Hill sets out the seasonal differences in deaths and, so far as then known, in cases. Except for the bearing upon them of seasonal case fatality, notification has added little, so far, to this aspect of whooping cough epidemiology. That the graphs suggest no law of incidence, no definite periodicity of recurrence, no characteristic case distribution and no rule in seasonal quiescence, may be due to the longer time-span required for their development. Certainly, neither in their annual nor in their biennial features do they show aught but a law unto themselves.

Dr. J. B. Russell, a former Medical Officer of Health of Glasgow, says (Public Health Administration in Glasgow. Studies in Epidemiology. Edited by A. K. Chalmers. Glasgow, 1905): "Estimated simply by the numbers of its victims, whooping cough is by a long way the most formidable infectious disease known to Glasgow. We might probably generalize and say the most formidable infectious disease of industrial cities. It shoots up into an epidemic at intervals of two to five years. . . . *But whooping cough never subsides to a low level. Its line of mean prevalence is high.*" This is true to-day. It is the high level of sub-epidemicity which is an outstanding feature of whooping cough, in the steady maintenance of which it contrasts with measles. Owing to this fact its endemicity is probably of more importance than its epidemic exacerbations recurring as they do at intervals normally much longer than those of measles. One sharply-defined epidemic only, and another of lower incidence, but more extended duration, occurred during the period (whooping cough graph, fig. 3). The first, commencing in April 1940, continued till the end of 1941, by which time it had fallen only to the mean level of six years' cases, having during the greater part of two years' epidemicity consistently maintained a high degree of prevalence. The second, commencing in December 1942, attained its first low peak in May 1943, and after a gradual decline and reascent, reached a slightly higher peak in May 1944, terminating as an epidemic by October of that year. For the rest of the six years, the incidence was that of a high endemicity, by no means of uniform level and subject to variations in weekly incidence not unlike those of its epidemic periods.

Inter-epidemic prevalence.—The low levels of incidence to which, between epidemics, whooping cough relatively and measles positively sink, have an interest for the epidemiologist

Section of Radiology

President—WHATELEY DAVIDSON, M.D., F.R.C.P., F.F.R.

(*January* 17, 1947)

Value of Tomography in Lesions of the Main Bronchi and their Larger Sub-divisions

By STANLEY NOWELL, M.B., F.F.R., D.M.R.

TOMOGRAPHY of the bronchi to demonstrate neoplasm and other lesions of the bronchi has been employed for several years.

The late E. W. Twining was one of the pioneers of its use for this purpose in this country. Bush has described cases of bronchial neoplasm demonstrated by tomography.

Hartley (1946) pointed out that in the diagnosis of lung carcinoma, owing to the diverse appearances on direct X-ray examination, the diagnosis of neoplasm is difficult and often only inferential. Even bronchoscopy may not be entirely successful. He stated that tomography is exceedingly accurate in the demonstration of carcinoma involving the bronchial wall, that one can assess whether bronchial carcinoma or mediastinal tumour is present and even, in some cases, differentiate lymphadenoma from lymphosarcoma.

The value of tomography is inadequately realized in this country.

G. W. Holmes has stated that the diagnosis of bronchial carcinoma depends entirely on the demonstration of deformity or obstruction of a bronchus and points out the value of tomography in showing definitely that there is an obstructing lesion of a bronchus. The late Tudor Edwards in 1945 mentions this use of tomography and Maurice Weinbren, 1946, "Manual of Tomography," London, illustrates some cases.

I shall discuss the value of tomography in lesions of the main bronchi and their larger divisions.

In tomography of the normal bronchi it is possible to show the trachea, right and left main bronchi and both upper lobe bronchi as far as their main divisions.

The lower lobe bronchi are seen for about two inches down to their main divisions and the middle lobe bronchus is also seen.

In the lateral tomograph the lower main bronchus is seen also the pectoral and first dorsal. With suitable technique other smaller branches further out may be seen.

These are not usually all seen on one film since, owing to the varying densities, different techniques are necessary for the various parts of the thorax. A graduated aluminium filter has been found helpful. It prevents the lung fields from being blotted out when the mediastinum is adequately penetrated. By this means central and peripheral bronchi may be more easily shown on one film.

Lesions of or affecting the bronchi, if they are to be demonstrated by radiology, must cause some deformity of the lumen of the bronchus. These deformities usually give the following appearances: (1) Smooth narrowing; or (2) irregular nodular narrowing of the lumen; (3) projection of a single nodule into the lumen; (4) complete blockage of the bronchus, either V shaped or rounded; (5) the origin of the bronchus is blocked with only a small nick showing.

All of these changes are readily visible, on tomography, in the main bronchi and their larger divisions.

Lesions external to the bronchi may press on and deform them evenly or invade them. In the latter case the appearances are similar to intrinsic lesions.

These effects may be caused by a variety of lesions both benign and malignant, intrinsic and extrinsic.

INTRINSIC LESIONS

These are (1) *inflammatory lesions*, granulomatous in type. They are usually either tuberculous or syphilitic (gumma).

Tuberculous lesions are usually from a direct extension or inhalation implantation from a lung cavity, occasionally in children from a lymph node. Œdema and nodular tubercle-formation occur, causing local emphysema or atelectasis. Oechsli states that they might be demonstrated by tomography or lipiodol. In practice there is usually a lung lesionp resent—cavity or infiltration—to suggest the diagnosis..

Syphilis.—One of the three main types of syphilitic lesion of the lungs is the gumma. It is usually near the hilum, peribronchial. The clinical signs are mild and of insidious onset. Serology is positive and it responds to anti-specific therapy. Sputum is negative for tubercle bacilli and for fungus.

at cultivating the immunizing process of which they have ever been the active, and in this respect collectively speaking, beneficent agents. Until this can be reliably effected by the promising prophylaxis of the immunologists, the path of still further fostering the natural course, the diseases themselves exhibit must be followed. Since the passing of the Public Health Act of 1875 the annual mortality they exact has fallen for each from over 400 to about 30 per million population, unaccompanied, so far as we can judge, by any corresponding or even positive fall in prevalence. This, the most signal feature in their behaviour, brings into striking relief the epidemiological importance of their case-fatality and marks the goal of the inevitable partnership they have imposed upon the human race, a more benign schooling to their wellnigh universal endemic-epidemic sway.

Dr. J. Alison Glover: Colonel Butler has, I think, triumphantly vindicated the epidemiological value of the notification of both diseases. Its practical value has, of course, been somewhat obscured during the war years by the shortages in medical, nursing and health visitor staffs and will become more obvious as these are restored to full strength.

In the decennium in which I began to study medicine, on an average 12,500 persons died each year of measles, and 11,500 of whooping cough. In the decennium ended 1945 the corresponding averages were 986 and 1,284. These impressive figures represent the saving each year of many thousands of lives and also a much lower incidence of those complications which, even when they do not kill, so often permanently damage health. There is little doubt that the immediate deaths form only a part of the mortality ultimately due to these two diseases.

The case fatality of measles, though it has varied greatly in different epidemics, used to be reckoned at about 4%. In 1945, though this was an epidemic year and 446,828 cases were notified, it was only 0·16%, about one-seventh of the immediate fatality rate of whooping-cough in the same year. Contrast this with 1918 when a modified system of notification (of the first case only in each family) was enforced, 414,346 cases were then notified, though of course there were many more. The number of deaths was 9,856 (nearly fourteen times as many as in 1945). Even if we assume that on average two cases occurred in each family, though probably this would over-estimate the actual number, the fatality rate must have been many times as great as that of 1945[1]. Colonel Butler has pointed out the very interesting sex ratio in the relative mortalities of the two diseases. It is an interesting point which I have not seen emphasized elsewhere that another disease, bacillary dysentery, resembles measles in that male infants and young boys show a higher notification of, and a much higher mortality from, dysentery than female infants and young girls, although in dysentery this higher young male incidence is much more pronounced and persists to a later age.

---

[1] Rep. of Chief Medical Officer of the Ministry of Health, 1945, 4. H.M.S.O. 1947.

Section of Radiology

President—WHATELEY DAVIDSON, M.D., F.R.C.P., F.F.R.

(*January* 17, 1947)

Value of Tomography in Lesions of the Main Bronchi and their Larger Sub-divisions

By STANLEY NOWELL, M.B., F.F.R., D.M.R.

TOMOGRAPHY of the bronchi to demonstrate neoplasm and other lesions of the bronchi has been employed for several years.

The late E. W. Twining was one of the pioneers of its use for this purpose in this country. Bush has described cases of bronchial neoplasm demonstrated by tomography.

Hartley (1946) pointed out that in the diagnosis of lung carcinoma, owing to the diverse appearances on direct X-ray examination, the diagnosis of neoplasm is difficult and often only inferential. Even bronchoscopy may not be entirely successful. He stated that tomography is exceedingly accurate in the demonstration of carcinoma involving the bronchial wall, that one can assess whether bronchial carcinoma or mediastinal tumour is present and even, in some cases, differentiate lymphadenoma from lymphosarcoma.

The value of tomography is inadequately realized in this country.

G. W. Holmes has stated that the diagnosis of bronchial carcinoma depends entirely on the demonstration of deformity or obstruction of a bronchus and points out the value of tomography in showing definitely that there is an obstructing lesion of a bronchus. The late Tudor Edwards in 1945 mentions this use of tomography and Maurice Weinbren, 1946, "Manual of Tomography," London, illustrates some cases.

I shall discuss the value of tomography in lesions of the main bronchi and their larger divisions.

In tomography of the normal bronchi it is possible to show the trachea, right and left main bronchi and both upper lobe bronchi as far as their main divisions.

The lower lobe bronchi are seen for about two inches down to their main divisions and the middle lobe bronchus is also seen.

In the lateral tomograph the lower main bronchus is seen also the pectoral and first dorsal. With suitable technique other smaller branches further out may be seen.

These are not usually all seen on one film since, owing to the varying densities, different techniques are necessary for the various parts of the thorax. A graduated aluminium filter has been found helpful. It prevents the lung fields from being blotted out when the mediastinum is adequately penetrated. By this means central and peripheral bronchi may be more easily shown on one film.

Lesions of or affecting the bronchi, if they are to be demonstrated by radiology, must cause some deformity of the lumen of the bronchus. These deformities usually give the following appearances: (1) Smooth narrowing; or (2) irregular nodular narrowing of the lumen; (3) projection of a single nodule into the lumen; (4) complete blockage of the bronchus, either V shaped or rounded; (5) the origin of the bronchus is blocked with only a small nick showing.

All of these changes are readily visible, on tomography, in the main bronchi and their larger divisions.

Lesions external to the bronchi may press on and deform them evenly or invade them. In the latter case the appearances are similar to intrinsic lesions.

These effects may be caused by a variety of lesions both benign and malignant, intrinsic and extrinsic.

INTRINSIC LESIONS

These are (1) *inflammatory lesions*, granulomatous in type. They are usually either tuberculous or syphilitic (gumma).

Tuberculous lesions are usually from a direct extension or inhalation implantation from a lung cavity, occasionally in children from a lymph node. Œdema and nodular tubercle-formation occur, causing local emphysema or atelectasis. Oechsli states that they might be demonstrated by tomography or lipiodol. In practice there is usually a lung lesionp resent—cavity or infiltration—to suggest the diagnosis..

Syphilis.—One of the three main types of syphilitic lesion of the lungs is the gumma. It is usually near the hilum, peribronchial. The clinical signs are mild and of insidious onset. Serology is positive and it responds to anti-specific therapy. Sputum is negative for tubercle bacilli and for fungus.

Male, aged 57. Admitted as ? perforation. Referred for barium meal. This was negative. At barium meal the left lower lobe was seen to be collapsed. Wassermann strongly positive.

Subsequent tomograms showed a narrowing of the left lower main bronchus just below the upper lobe branch (figs. 1 and 1A).

In the lateral tomogram the narrowing is clearly seen for a cm. or so (figs. 2 and 2A). This was confirmed by bronchoscopy where the narrowing was again seen. The wall was like old granulation tissue, with pale mucous membrane, uniform surface with no bleeding or oozing. ? a gumma.

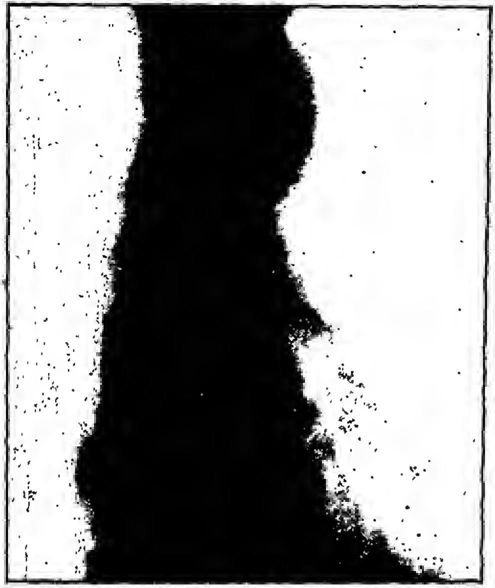


FIG. 1.

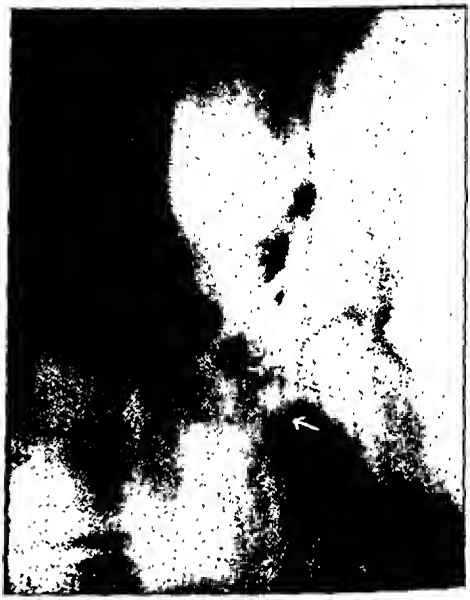


FIG. 2.

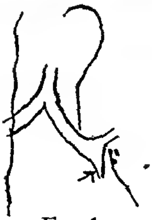


FIG. 1A.

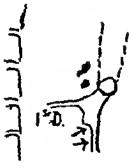


FIG. 2A.

FIG. 1.—Gumma of bronchus. Tomogram. Narrowing of left lower lobe bronchus near its origin.

FIG. 2.—Same patient. Lateral view.

FIGS. 1A and 2A.—Diagram of tomograms showing narrowing of the left lower lobe bronchus just below first dorsal origin. The narrowing is clearly demonstrated in the lateral tomogram.

He was treated with anti-specific therapy with much clinical improvement in two months. A direct film taken three months later showed the left lower lobe was nearly fully expanded.

A few months later he was admitted to the mental hospital as a case of general paresis. A film then showed the left lower lobe to be fully expanded.

A case similar to this, with post-mortem confirmation, was described by Stevens and Hudson in 1934 (not tomogram).

Pearson cites lobar atelectasis occurring in syphilis.

(2). *Neoplasms.*—Benign and some types of *malignant neoplasms* produce the appearance of type three or four in the bronchus (*see* previous list)

Bronchoscopy is necessary to differentiate and section is advisable since an adenoma may be malignant.

Malignant neoplasms may give any of the five types of deformity but types four and five are, I think, usually definite evidence of a carcinoma bronchus.

If one bronchus is not seen my experience is that the finding must be ignored and the examination repeated. It is usually due to a technical fault. However if one bronchus is not seen but the adjacent larger or smaller bronchus shows a narrowing or deformity, then the findings may be accepted as a definite bronchial block with invasion of the adjacent bronchi as demonstrated. The following cases show well such a condition.

W. (fig. 3).—Collapse of left lower lobe. Tomogram: Left lower lobe bronchus not seen. Left main narrowed and deformed. Infiltrating neoplasm of bronchus. Patient died three months later.

R. O. (figs. 4 and 4A, and 5 and 5A).—Left lower lobe bronchus not seen on tomogram. Left

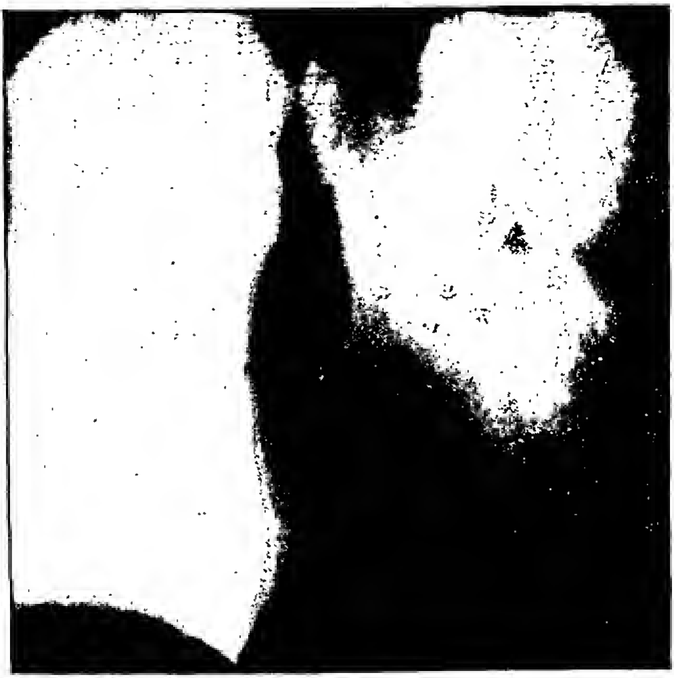


FIG. 3 Case W.).—Left lower bronchus not seen, left main narrowed and deformed. Infiltrating neoplasm of bronchus.

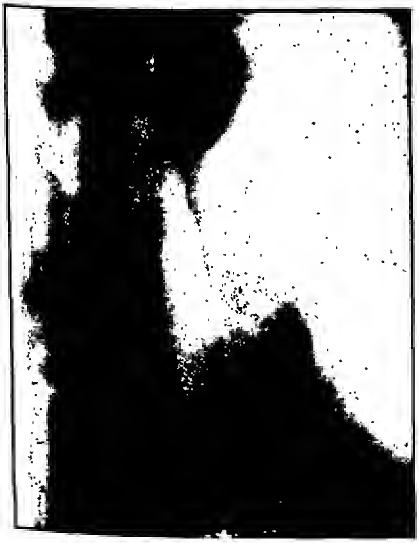


FIG. 4.

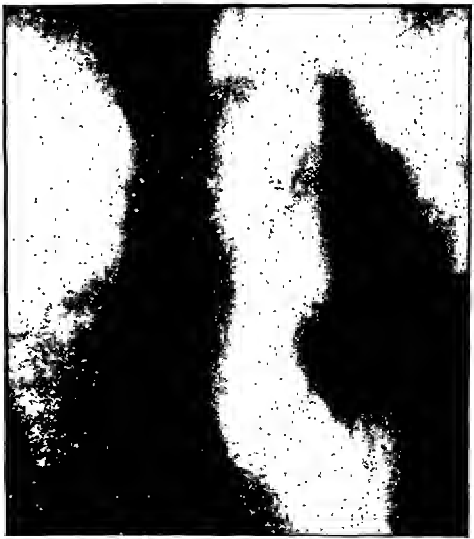


FIG. 5.

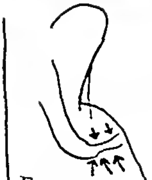


FIG. 4A.

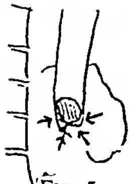


FIG. 5A.

FIG. 4 (Case R. O.).—Tomogram. Left lower bronchus not seen. Left upper bronchus somewhat irregular. Compare with lateral tomogram, fig. 5.

FIG. 5.—Lateral tomogram of same case as fig. 4. Note that the blockage of the left lower main bronchus is clearly demonstrated at origin.

FIGS. 4A and 5A.—Diagram of tomograms of Case R. O. Note narrowing of left upper lobe bronchus indicating spread of invasion.

Male, aged 57. Admitted as ? perforation. Referred for barium meal. This was negative. At barium meal the left lower lobe was seen to be collapsed. Wassermann strongly positive.

Subsequent tomograms showed a narrowing of the left lower main bronchus just below the upper lobe branch (figs. 1 and 1A).

In the lateral tomogram the narrowing is clearly seen for a cm. or so (figs. 2 and 2A). This was confirmed by bronchoscopy where the narrowing was again seen. The wall was like old granulation tissue, with pale mucous membrane, uniform surface with no bleeding or oozing. ? a gumma.

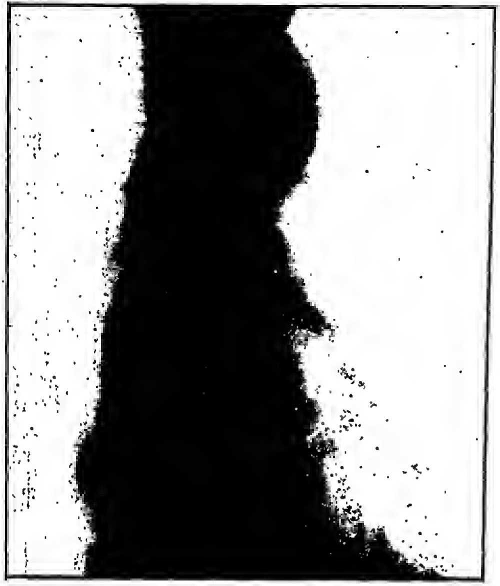


FIG. 1.

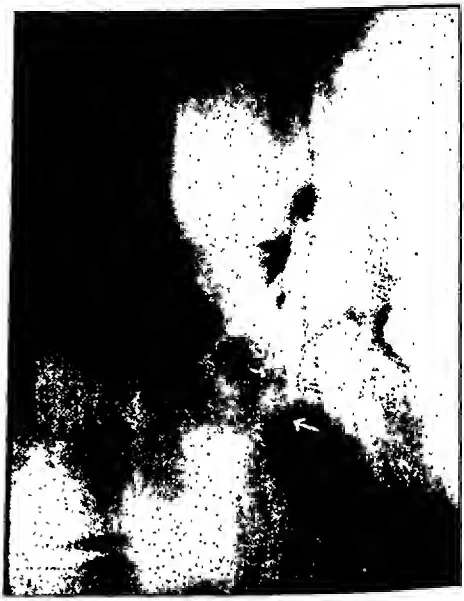


FIG. 2.

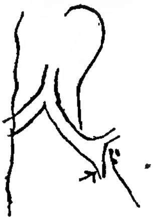


FIG. 1A.

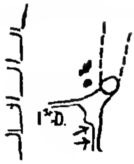


FIG. 2A.

FIG. 1.—Gumma of bronchus. Tomogram. Narrowing of left lower lobe bronchus near its origin.

FIG. 2.—Same patient. Lateral view.

FIGS. 1A and 2A.—Diagram of tomograms showing narrowing of the left lower lobe bronchus just below first dorsal origin. The narrowing is clearly demonstrated in the lateral tomogram.

He was treated with anti-specific therapy with much clinical improvement in two months. A direct film taken three months later showed the left lower lobe was nearly fully expanded.

A few months later he was admitted to the mental hospital as a case of general paresis. A film then showed the left lower lobe to be fully expanded.

A case similar to this, with post-mortem confirmation, was described by Stevens and Hudson in 1934 (not tomogram).

Pearson cites lobar atelectasis occurring in syphilis.

(2). *Neoplasms.*—Benign and some types of *malignant neoplasms* produce the appearance of type three or four in the bronchus (*see* previous list)

Bronchoscopy is necessary to differentiate and section is advisable since an adenoma may be malignant.

Malignant neoplasms may give any of the five types of deformity but types four and five are, I think, usually definite evidence of a carcinoma bronchus.

If one bronchus is not seen my experience is that the finding must be ignored and the examination repeated. It is usually due to a technical fault. However if one bronchus is not seen but the adjacent larger or smaller bronchus shows a narrowing or deformity, then the findings may be accepted as a definite bronchial block with invasion of the adjacent bronchi as demonstrated. The following cases show well such a condition.

W. (fig. 3).—Collapse of left lower lobe. Tomogram: Left lower lobe bronchus not seen. Left main narrowed and deformed. Infiltrating neoplasm of bronchus. Patient died three months later.

R. O. (figs. 4 and 4A, and 5 and 5A).—Left lower lobe bronchus not seen on tomogram. Left

These show the extent of invasion which may be present without collapse or even much hilar increase.

Any case with the least suspicion of carcinoma should be tomographed.

Tomography in More Peripheral Lesions

In the more peripheral lesions a malignant infiltration will invade the smaller bronchi and cause narrowing in parts. The following cases show such invasion:

D. M/62.—Weakness, cough, weight loss. Direct: Patchy infiltration in axillary segment. Tomogram: Right upper and lower main bronchi well seen and clear. Junction of right axillary and apical ill-defined. Axillary narrow. Probably carcinoma with lymphatic spread. Post-mortem: Carcinoma at site shown. Two small liver metastases.

R. M. M/57.—Weight loss. B.S.R. 104. No definite chest symptoms. Left sciatic pain one week. Direct: Irregular shadow close to right hilum just posterior to mid-plane (fig. 6). Tomogram: Apical branch is distorted and irregular. Opinion that it is a malignant lesion on these grounds (fig. 6A). One month later right lower lobe commencing collapse. Diaphragm rising, right. Died. No post-mortem allowed.

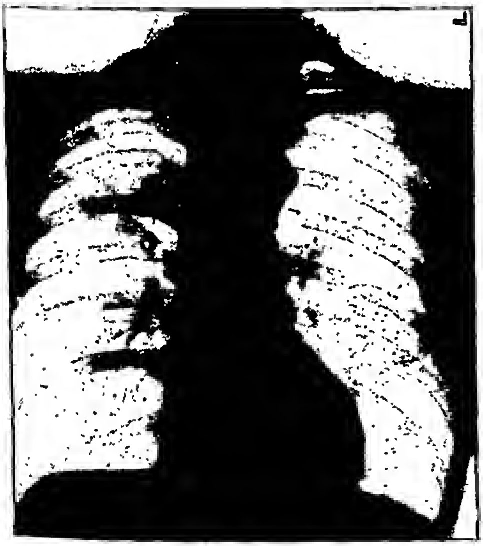


FIG. 6.

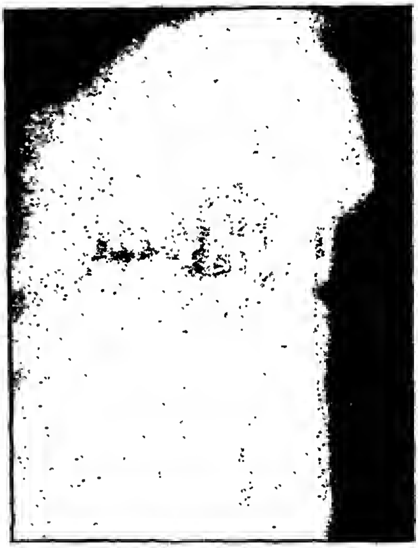


FIG. 6A.

FIG. 6 (Case R. M.).—Direct film. Irregular fairly well defined shadow close to right hilum and just posterior to mid-plane.

FIG. 6A.—Tomogram of case in fig. 6. Irregularity and distortion of the right apical branch is demonstrated. This branch is lying in the shadow.

R. J. M/62.—Silicotic; on compensation. From S. Africa. Direct film: Shadow 2 cm. size in upper lobe just anterior to main bronchi. D.9 collapsed and erosion in twelfth rib head.

Tomogram: Main bronchi clear. Apical and axillary bronchi not narrowed or distorted, though they are lying just behind and close to the shadow. In a lateral tomogram the pectoral branch is seen just below the shadow in the same plane. It shows no narrowing or displacement. Probably a malignant alveolar lung lesion.

At post-mortem a necrotic tumour, microscopically a carcinoma, was found at the site of the shadow. The bone lesions were secondaries.

The view is put forward that if a lung infiltration is malignant the bronchi close to or in it will be narrowed in parts and some blocked. In a case of tuberculosis they were not so affected and the infiltration was more discrete on tomography.

With small or medium-sized tumour shadows in the lungs, clear of the main bronchi, tomography may be helpful, if the shadows of the smaller bronchi are studied. With a upper lobe bronchus a little irregular. Note, however, that the irregular blockage of the left lower lobe bronchus is shown in the lateral tomogram. If not seen in an a.p. tomogram narrowing of a lower main bronchus may be seen in a lateral tomogram. Often the whole length of the narrowing and irregularity of the lumen is seen in a lateral tomogram.

Tomograms also often disclose invasion around adjacent main bronchi and even the main bronchus of the opposite side may be invaded. Such wide invasion was shown by tomography in the following case.

C.—Was admitted with œsophageal obstruction. There was an infiltrative lesion of the œsophagus. It was also noted that the left lower lobe was collapsed.

Tomograms showed blocking of the left lower bronchus and infiltration of right and left main bronchi.

Post-mortem confirmation of bronchial carcinoma with secondary spread and invasion of outer walls of œsophagus.

On tomography alone I know of no method of absolutely distinguishing an inflammatory lesion or benign or malignant neoplasm of the bronchi. Even bronchoscopy may not be able definitely to decide. However, from tomography very suggestive evidence is obtained.

(1) A single nodule is a neoplasm, benign or malignant. (2) A complete V block, especially at origin is almost certainly a bronchial carcinoma. (3) A bronchus not seen, but adjacent bronchi narrowed, is a malignant growth with wide spread. (4) A narrowed bronchus with other bronchi also narrowed means a carcinoma with wide spread.

This is a measure of the value of tomography in assessing amount of invasion.

EXTRINSIC LESIONS

These are mainly glandular; Hodgkin's disease, lymphosarcoma, leukæmias, &c., and also thymic tumours and benign mediastinal tumours.

These usually cause extrinsic pressure effects. If no bronchial invasion is seen then a malignant lesion of the bronchus can be ruled out, and the diagnosis of mediastinal tumour made on other radiological and clinical grounds. Possibly the tomogram may bring to light some faint calcification not previously seen, suggestive of dermoid.

Hartley (1946) pointed out that lymphosarcoma, though extensive, does not commonly compress or invade the bronchi, whereas Hodgkin's disease usually displaces or compresses the bronchi. By such signs a differential diagnosis is possible.

However, both of these can invade the bronchi causing a granulomatous occlusion and atelectasis. In such cases the appearances are those of intrinsic invasion and even the extent of invasion is no guide since bronchial carcinoma, as previously demonstrated, may have wide invasion. However, with malignant mediastinal tumour the invasion, one finds, is usually more hazy and ill-defined, often with gross distortion of channels.

Tomography in Bronchial Lesions with No Lobar Collapse

Nearly all the cases so far have been fairly obvious, having gross atelectasis or large shadows. Even in such cases tomography may give the exact cause of the atelectasis or, conversely, rule out a bronchial neoplasm.

Even when there is no real atelectasis and slight dubious hilar enlargement and possibly a little hæmoptysis tomography can very definitely help.

About 10% of all ultimately proved carcinoma bronchi will be seen in this early stage, so it is important to do tomograms on them. Cases of this type are described.

H. J. M/46.—Few months slight dyspnœa. Recent slight hæmoptysis. Direct film: Irregular, not very dense increase in right hilum. No lobar collapse.

Tomograms: Irregular narrowing of right lower main bronchus for ½ in. above right middle. Well seen on lateral tomogram where slit-like narrowing is shown.

Bronchoscopy: papilliferous tumour at site. Thoracotomy and pneumonectomy. Tumour could not be completely removed. Died a year later.

J. G. M/47.—Dyspnœa 4/12. Chest pain. No hæmoptysis. Direct: Left hilum enlarged, fine processes from it. No collapse of lobes.

Tomogram: Left main narrowed and irregular. A more extensive lesion than one would expect is shown.

He soon developed an abscess and later bronchial obstruction.

time he could be quickly transferred to the person or department most suitable. On the other hand, if a patient could be shown quickly to have a tumour involving the mediastinum, with no evidence of primary lung disease and a presumptive diagnosis excluding benign tumours and cysts, such a case could be readily dealt with by the radiotherapists; for radiation therapy would be likely not only to prove beneficial but to be of diagnostic value. since the nature of the response of the tumour to radiation afforded this information. In other words in cancer treatment it was sometimes more important to decide quickly whether or not to treat the patient than it was to establish the exact academic diagnosis.

Dr. R. Kemp Harper disagreed with the statement made by Dr. Peter Kerley that tomography was of little value in the diagnosis of peripheral carcinoma of the lung. He pointed out that the size, position, density and limits of the opacity in the lung could be more clearly defined by the use of tomography, and all these points were of great importance in differentiation. In connexion with the diagnosis of enlarged tracheobronchial glands secondary to carcinoma of the lung, he drew attention to the fairly constant appearance of a smooth oval or circular density at the right tracheobronchial angle which was caused by the azygos vein and should not be mistaken for an enlarged gland.

Dr. Thomas Lodge suggested that it was well to remember that there were other structures in the lung besides the bronchi and that different tomographic techniques in a given case should be employed in order to demonstrate the other structures, for example, the displacement of the lung vessels by benign tumours.

Dr. A. Elkeles (in reply): The described pulmonary changes associated with mitral stenosis are not so rare as Dr. Kerley suggests. Since cardiologists usually obtain their information by screening only, these pulmonary nodular infiltrations may have easily escaped recognition. Furthermore these calcified nodular infiltrations have been interpreted in the past as calcified tuberculosis. Evidence can be found in the literature of such cases having been sent unnecessarily for prolonged sanatorium treatment.

My second patient and some cases described in the literature showed no clinical or radiological evidence of pulmonary congestion, which invalidates the theory that these bony nodules are the result of long-standing passive congestion. The history of rheumatic pneumonia and pleurisy in these patients and in particular the microscopic findings of specific rheumatic changes in the lungs are in support of our theory of these ossified nodules being the late stage of rheumatic pneumonia.

I agree with Dr. Lodge's remarks, that the lung changes are primarily vascular in nature, which lends further support to the theory, that rheumatic fever belongs probably to the more severe type of vascular allergy.

Disseminated Ossified Nodules in the Lungs Associated with Mitral Stenosis

By A. Elkeles, M.D.

Nodular calcifications in the lungs are generally interpreted as evidence of healed primary or post-primary tuberculosis. Recent investigations by mass-radiography indicate that this current concept of pulmonary calcifications may have to be revised at least to some extent. Pulmonary calcifications were found in a considerable number of cases, in which no evidence of past or present tuberculosis could be found, and in which the Mantoux test proved negative. As causative agents of the so-called non-tuberculous calcifications in the lungs, infection with *Ascaris lumbricoides*, coccidiomycosis and aspergillosis have been suggested, but convincing evidence for this assumption is still lacking. Zwerling and Palmer (1946) on examining a total of 6,199 student nurses by mass-radiography in the central eastern states of America, found pulmonary calcifications in 698. These authors suggest that infection with *Histoplasma capsulatum* may be responsible for a large number of pulmonary calcifications and base their assumption mainly on the result of skin tests. These revealed that 494 out of 698 cases were histoplasmin positive, whereas only 57 were tuberculin positive and 109 positive to histoplasmin and tuberculin, the remaining 38 were negative to both. Whether Palmer's findings may only apply to certain areas in the United States, where infection with *Histoplasma capsulatum* may be prevalent, or whether it will prove to be of wider significance, remains to be seen, when mass-radiography will be performed on a wider scale.

The purpose of this paper is to draw attention to a special type of pulmonary nodular calcifications occasionally met with in mitral stenosis. Although the X-ray appearances show a close resemblance to calcified pulmonary tuberculosis caused by hæmatogenous spread, the macroscopical and microscopical examination of the lung in these cases reveal no evidence of tuberculosis and most of the nodular lesions were found to consist of true bone.

E. Wagner was the first to report on bone formations in the lungs as far back as 1859, when he published a case of a female, 25 years of age, who died of dropsy and in whom he found numerous bones in the lungs. In 1862 Heschl published a paper on osteoides in the non-malignant tumour the bronchi close to the shadow will be displaced away from the shadow. If the shadow is due to a malignant tumour the bronchi running through it are narrowed or occluded due to invasion. Those close to it are neither displaced nor narrowed.

An exception to this is a chronic abscess. In one case with a chronic thick-walled abscess, proved by operation, the tomogram shows a severe narrowing of the left upper lobe bronchus below the main shadow, close to the origin of this bronchus. This was misinterpreted at the time as a carcinoma of the upper lobe. The explanation appears to be that in contracting the abscess had constricted the upper lobe bronchus by fibrous bands surrounding it.

CONCLUSIONS

By the use of tomography in both antero-posterior and lateral planes and by varying technique and methods to suit the individual case a good view of the main bronchi and many of the smaller bronchi may be obtained without disturbance to the patient and without introducing opaque media into the bronchi.

With the bronchi thus visualized changes in their lumen from intrinsic or extrinsic lesions are demonstrable. In many cases the changes so demonstrated are a sufficient basis for a definite diagnosis. However, in general, bronchoscopy is necessary to determine the nature of the lesion. Tomography and bronchoscopy are thus complementary. Tomography is, however, of great value in demonstrating the site of a lesion prior to bronchoscopy and in cases where bronchoscopy is negative tomography may demonstrate a lesion.

Tomography is valuable in showing the extent of invasion of the bronchi, invasion of adjacent and even the contralateral bronchus being demonstrable.. It may be of great value in differentiating various types of mediastinal lesions.

If the smaller bronchi are adequately studied by tomography a valuable clue as to the nature of more peripheral lung lesions may be obtained. In such cases careful attention must be given to these bronchi to see whether they are narrowed, blocked, distorted or displaced.

In cases which show a slight or moderate hilar enlargement with no lobar collapse or even no commencing atelectasis tomography is of extreme value. In such cases it will very often demonstrate a lesion of the main bronchus, showing both the site and extent of the lesion and very often giving a valuable clue as to its nature.

REFERENCES

BUSH, G. B. (1938) *Brit. J. Radiol.*, 11, 611.
EDWARDS, A. T. (1946) *Thorax*, 1, 1.
HARTLEY, J. B. (1946) *Proc. R. Soc. Med.*, 39, 531.
HOLMES, G. W. (1942) *Amer. J. Roentgenol.*, 48, 425.
LYONS, C. G., BROGAN, A. J., and SAWYER, J. G. (1942) *Amer. J. Roentgenol.*, 47, 877.
PEARSON, R. S. B., and DE NAVASQUEZ, S. (1938) *Brit. J. vener. Dis.*, 14, 243.
STEVENS, H. R., and HUDSON, W. A. (1934) *Radiology*, 22, 339.
TWINING, E. W. (1938) A Text Book of X-ray Diagnosis. London, 1, 371.

Dr. G. Simon inquired whether the speaker had found tomography of any value in deciding on the operability or otherwise of pulmonary neoplasms.

Dr. P. Kerley; Accurate tomography requires a considerable amount of time and the personal attention of a radiologist. It can be of help in some cases of malignant disease of the lungs, but I would not agree that it should be employed as a primary diagnostic measure.

The lung is one of the commonest sites of carcinoma in men and the only prospect of cure lies in early surgery. Bronchoscopy is by far the quickest and most reliable method of establishing a diagnosis once suspicion of the condition is raised, either by symptoms or the finding of an abnormal radiological shadow.

I find tomography of more help in seeking for unsuspected enlarged mediastinal glands secondary to primary carcinoma of the lung.

Dr. J. Blair Hartley expressed the view that although tomography required the same personal attention to the case, and frequently formed but part of the very detailed investigations necessary, nevertheless it was incorrect to assume that carefully-devised routine tomographic investigations were not often of the greatest value. One knew, from experience in a very large number of cases, the levels between which the mediastinal shadow and the trachea and main bronchi must lie. A series of sections taken through this "area" must, therefore, produce information concerning the position and appearance of the major bronchi. Thus, it is frequently possible to determine, within a few moments, whether an acknowledged tumour is of mediastinal or pulmonary origin. In a large radiotherapy centre it was not always necessary to make a precise diagnosis before dealing with the case, for if a patient could be rapidly shown to be untreatable by radiation therapy, instead of wasting spread to different parts of the lungs by hæmoptysis. Since there is neither evidence of cavitation nor any history of hæmoptysis, it may reasonably be assumed that the widespread calcified nodular infiltrations are of the same type as in the previous case. Furthermore the diagnosis of pneumonia and pleurisy by her doctors during the acute attack of rheumatic fever suggests that according to our present knowledge the patient was suffering from rheumatic pneumonitis and pleurisy. The same probably applies to Derischanoff's case, who suffered from severe pneumonia for over two and a half months, four years prior to his admission to hospital. The history of pneumonia during the course of rheumatic fever may be taken as further evidence in support of our theory that ossified pulmonary nodules in rheumatic valvular disease are the late results of rheumatic pneumonitis.

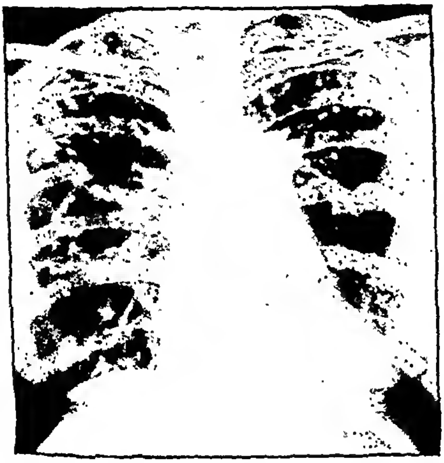


FIG. 1.—Mitral stenosis with disseminated nodular spacities in both lung fields.

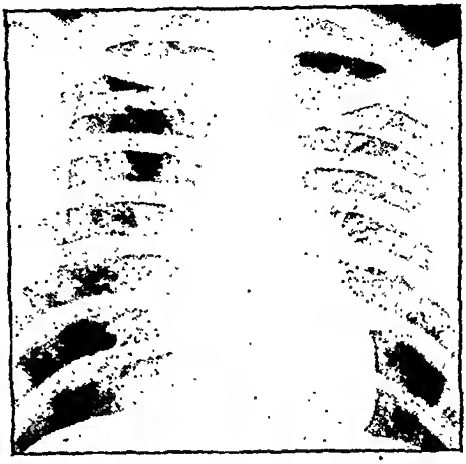


FIG. 2.—Chronic calcified miliary pulmonary tuberculosis.

With regard to the radiological diagnosis of the pulmonary lesions, it is obvious that calcified nodular infiltrations as such do not represent a characteristic feature, as they may be met with in other conditions. Indeed the pulmonary lesions show a certain resemblance to calcified chronic miliary tuberculosis. It is in particular the association of the pulmonary lesions with mitral stenosis which should raise doubts as to the tuberculous character of the nodular calcifications. Pulmonary tuberculosis is a common complication in congenital heart disease, but is only rarely met with in mitral stenosis. The absence of extensive calcified mediastinal glands or of post-primary parent lesion or lesions in the lungs may also be taken as evidence against the tuberculous character of the calcified nodules.

Since calcified miliary tuberculosis is extremely rare, strong evidence for the tuberculous origin of miliary, pulmonary calcifications is required as for instance the detection of tubercle bacilli or calcified nodules in spleen, liver or other organs or the involvement of skin, bones, joints or genito-urinary tract, &c.

In the following case we can compare the pulmonary lesions of calcified miliary tuberculosis with those of the calcified nodules in mitral stenosis.

Male, 34 years of age, has a history and radiological evidence of healed tuberculosis of the right hip-joint, and a still active tuberculosis of the right shoulder-joint with a discharging sinus. Radiogram of his chest taken on 13.12.46 reveals numerous, minute shot-like calcareous deposits in both lungs, which show an almost symmetrical distribution over the middle and upper lung fields. An old Ghon's focus is seen in the left lower zone with calcification of the draining hilar glands. The left costophrenic angle is slightly obscured and suggestive of healed pleurisy (fig. 2).

The distinguishing features of the chest radiograms of the two conditions are:

In mitral stenosis.—The calcified nodules vary from pinhead to large pea size. They show various shades of density, are not always discrete and have a tendency to coalesce. The nodules are distributed over the central lung fields as well as the periphery.

lungs in a male 26 years old with chronic endocarditis. Derischanoff in 1930 described a case of a male 21 years of age, who died of cardiac failure due to mitral stenosis and incompetence. On post-mortem examination multiple tuberous osteomata were found in both lungs, more numerous in the lower lobes, but also present in both apices. Four years prior to his admission to hospital he had suffered from pneumonia lasting for over two and a half months. Salinger (1932) was the first to recognize the relationship of pulmonary bony nodules and mitral stenosis. In recent years several cases of this strange co-existence have been reported in the American and continental literature. The only case published so far in this country is by Elkeles and Glynn (1946). In this paper evidence was produced for the probability of the pulmonary ossified nodules to be the end-result of rheumatic pneumonia and not, as hitherto believed, the outcome of long-standing passive congestion of the lungs in mitral stenosis.

The patient was 32 years of age and suffering from advanced mitral stenosis with auricular fibrillation and passive congestion of the lungs. Chest radiograms confirmed the clinical diagnosis of mitral stenosis with passive pulmonary congestion. Both lung fields were scattered with numerous densely opaque nodules of pinhead to small pea size. The right lower lobe was predominantly involved and particularly its periphery. The nodules were well defined and the larger ones were mulberry-like in shape. No nodular infiltrations were seen in the apices. No calcified mediastinal glands and no evidence of primary or post-primary lesion or lesions were present. The radiological diagnosis of non-tuberculous calcified bony nodules associated with mitral stenosis was confirmed by post-mortem examination nine months later. The microscopical examination of the pulmonary nodules proved them to consist of bone of the woven type and intra-alveolar in position.

Bone formation in the lungs is occasionally met with in old men, but the bone is formed in the interstitial tissue and not in the parenchyma of the lung. Pulmonary ossification is often met with in healed primary tuberculous lesions. In the primary focus the central area undergoes caseation and destroys the elastic framework of the lung and healing proceeds by the deposit of calcium salts in the caseous material, bone tissue is formed in the periphery from the specific connective tissue by metaplasia, thus creating a bony shell, which walls off the diseased area. The healed primary focus can therefore be distinguished on microscopical examination from the ossified nodules in mitral stenosis by the destruction of the elastic framework of the affected area and by marginal ossification.

It is likely that the described pulmonary lesions have in the past often been interpreted as calcified tuberculosis on chest radiograms.

The second case to be reported here confirms this assumption.

A female, 43 years old, had severe tonsillitis at the age of 9 followed by rheumatic fever and complicated by pneumonia and pleurisy and valvular disease of the heart. When over fourteen years ago the first X-ray of the chest was taken, her lungs showed evidence of widespread calcified nodular infiltrations, which were then interpreted as healed pulmonary tuberculosis. No tubercle bacilli could be found in frequent sputum examinations. A radiogram of her chest taken in July 1946 shows a small aortic knob, a prominent pulmonary conus and an enlarged pulmonary artery, straightening of the middle segment of the left cardiac border. The left ventricle is somewhat enlarged, which may, however, only be apparent owing to the rotation of the heart, which sometimes takes place in right ventricular enlargement. Both lung fields are scattered with numerous nodules of varying density, size and shape. The nodular opacities are most widespread in the upper zones, even involving the apices. The middle zones show somewhat less involvement, and some nodules are visible in the region of the right cardiophrenic angle. The left lower zone is almost clear. The nodules vary from a pinhead to a pea. On close inspection many of the small nodules are round and discrete, the larger ones are often mulberry-like in shape and some have translucent areas in their centre, others coalesce with neighbouring nodules. Much fibrosis is visible in the upper zone. Calcified hilar glands are conspicuously absent (fig. 1).

Clinically the patient has a loud rumbling diastolic murmur with presystolic accentuation at the apex, P2 is accentuated. An E.C.G. reveals right preponderance and flattening of T waves in lead 3. The loud diastolic murmur as such is no indication of the severity of mitral stenosis. The patient shows no evidence of cardiac failure and is leading an active life; she is still able to climb three flights of stairs without appreciable dyspnœa. The patient has no history of pulmonary or extra-pulmonary tuberculosis. The absence of calcified hilar glands makes the pulmonary lesions unlikely to be the result of a primary infection. Widespread dissemination of tuberculous lesions in the lungs arising from post-primary infection, whether hæmatogenous or bronchogenic, originate mainly from cavitation or are

JOINT DISCUSSION No. 2

Section of Surgery with Section of Radiology

Chairman—ERNEST FINCH, M.D., M.S., F.R.C.S.
(President of the Section of Surgery)

[*January* 1, 1947]

DISCUSSION ON THE TREATMENT OF CANCER OF THE TONGUE

Sir Stanford Cade: My remarks are based on the observation of about 550 patients with malignant lesions in the mouth; of these, 380 were primarily tongue lesions. The period covered is just under thirty years and it is twenty-two years since I first used radium in the treatment of lingual cancer.

What is our knowledge to-day of cancer of the tongue as a disease entity? What are the accepted forms of treatment, and what hope is there for a patient to survive to his allotted span?

Cancer of the tongue has undergone a change in its natural history in our generation, but evolutionary changes are slow and, to those who are part of them, imperceptible. It may therefore be useful to reflect on the main changes. This disease was usually associated with poverty—it is by no means exclusively so to-day, although its association with bad oral hygiene and gross dental sepsis remains of ætiological significance. The sex incidence in the past twenty years has altered from a 10% incidence in women to nearly 20% of the total number of cases of cancer of the tongue, and in some countries, for instance Sweden, it is nearly 40%. The incidence of the disease has shown a decline for the past thirty-five years, but not simultaneously in all age-groups; thus at ages under 65 the decline has been continuous since 1911, but for the 65 to 74 decade it did not begin till 1935; and not till 1940 was a fall registered in the age-group of 75 and over.

There is thus a relative and an absolute diminution in the incidence of the disease which is now the lowest in incidence of all sites. In England and Wales about 1,000 deaths a year are registered as due to cancer of the tongue; the computation of patients alive with the disease is very much more difficult; but even if the totals reach three times that figure, there are only 75 cases of cancer of the tongue to every million living persons. This low incidence has a great bearing on the organization of the treatment, if adequate treatment only is to be offered.

Factors which determine the choice of treatment.—The important factors which determine the choice and technique of treatment are the *site, extent,* and macroscopical *type* of the lesion; to a lesser extent the histological classification of the degree of malignancy. The presence or absence of enlarged cervical nodes vitally affects the prognosis but does not *per se* determine the treatment of the primary growth.

It is no longer necessary to emphasize that radiation is the first choice as a therapeutic measure for the primary growth. It is more profitable to indicate the place of surgery; it is also simpler to do so as the field of surgery has narrowed down to a few, well-defined indications. Providing adequate facilities and trained personnel are available, the primary lesion in all cases of cancer of the tongue should be treated by radiation with the exception of the following: (1) Where the lesion has transgressed the floor of the mouth and involved the mandible. (2) Where the entire tongue is involved in its anterior part down to the V of the circumvallate papillæ by a hard infiltrating growth. (3) In cases which have failed to respond to radiation either as an immediate failure with but slight regression of the lesion; or when recurrence of active disease takes place within a few months of treatment.

It should be noted that the earlier the lesion, the more suitable it is for radiation;

In calcified miliary tuberculosis.—The calcified nodules are discrete and more uniform in size and density. They mainly involve the central lung fields. There is usually evidence of primary or post-primary tuberculous lesions.

There are several other conditions in which calcified nodular opacities in the lungs may occur, e.g. pneumoconiosis, calcium metastasis, pneumomycosis, pulmonary hæmosiderosis and sarcoidosis, the history, clinical picture and laboratory investigations should assist in the differential diagnosis. Finally the miliary type of long-standing passive congestion of the lungs in mitral stenosis will be mentioned. According to Peter Kerley the combination of swollen end-on vessels and alveoli filled with heart-failure cells are responsible for the nodular opacities. Since the pulmonary vessels decrease in size towards the periphery, there is a corresponding decrease in the size of the spots, a feature which should help in the differential diagnosis from other miliary lesions and in particular from the above-described pulmonary lesions in mitral stenosis.

The described pulmonary changes in rheumatic valvular disease are not only of diagnostic interest, but if our theory of the pathogenesis of the ossified nodules could be confirmed, it would be further proof of the existence of specific rheumatic manifestations in the lungs.

POSTSCRIPT (6.5.47).—A third personal case has just been observed which shows the same nodular calcified pulmonary infiltrations in a long-standing case of mitral stenosis.

REFERENCES

DERISCHANOFF, S. M. (1930) *Frankfurt. Z. Path.*, 15, 485.
ELKELES, A., and GLYNN, L. E. (1946) *J. Path. Bact.*, 18, 517.
HESCHL, (1862) *Osterr. Z. prakt. Heilk.*, 8, No. 3.
KERLEY, P. (1938) A Text Book of X-ray Diagnosis. London, 1, 87.
SALINGER, H. (1932) *Fortschr. Röntgenstr.*, 46, 269.
WAGNER, E. (1859) *Arch. physiol. Heilk.*, 18, 411.
ZWERLING, H. B., and PALMER, C. E. (1946) *Radiology*, 47, 59.

Dr. P. Kerley: There should be a very sharp differentiation between calcified nodules and ossified nodules. In the case described by Dr. Elkeles the nodules were composed of true osseous tissue. Calcification occurs in the absence of a good blood supply.

We know from observation of traumatic vascular injuries that bone stimulation occurs with chronic venous stasis. I think this is a prominent factor in the development of osseous nodules in mitral stenosis. I would not agree that the infective agent in rheumatic fever is responsible for the osseous formation, since the condition is so rare and has not been described in aortic lesions of rheumatic origin.

Dr. Thomas Lodge thought that Dr. Elkeles had put his finger on the key to the problem in many cases of unusual opacity in the lung either calcareous or ossified nodules or even iron pigmentation. The pathologists now felt that there was a primary rheumatic condition of lung vessels not always associated with rheumatic endocarditis, and that changes in the intima of the vessels might lead to increased permeability to calcium and to the deposition of calcified and ossified nodules in the lung.

Dr. James Bull said that he thought pulmonary schistosomiasis should be considered in the differential diagnosis of small multiple calcified lesions in the lungs. He had seen a case about six years ago, a British soldier who had served in Egypt and had bathed in the Nile, who was suffering from a brain-stem lesion thought to be granulomatous in type. There was no evidence of syphilis or tuberculosis and an X-ray of the lungs showed a bizarre picture of multiple minute densely calcified foci. The case was never confirmed by autopsy and no calcified foci were seen in the bladder or rectum. Dr. Bull was very struck by the similarity of the X-ray appearances to the lung specimens illustrated in Shaw and Ghareeb's paper (1938). They had performed 282 autopsies on cases of schistosomiasis and at least 33% had pulmonary involvement and many of the lesions were calcified. *S. hæmatobium* was twice as common as *S. mansoni* and 11% showed mixed infection.

Dr. Bull suggested that this lesion might be seen in this country in the next few years as so many residents of these islands had served in the Nile Valley during the war. It was also possible that *S. japonicum* behaved in the same way although Dr. Bull knew of no reference confirming it.

REFERENCE

SHAW, A. F. B., and GHAREEB, A. A. (1938) *J. Path. Bact.*, 46, 401.

first for surface applications, and subsequently worked out by them for interstitial therapy, remains the simplest, the most useful and generally accepted method. As regards the total dose it has varied in our cases from 6,000 r to 9,000 r delivered in 168 hours; the dosage rate showed an equally wide range from 30-75 r/hr. For interstitial treatment an average of six days is now used.

As regards teleradium, a vast amount of clinical, physical and biological research has been done in the past fifteen years. The magnitude of the task can be illustrated by the problems which the treatment presents: total dose, dosage rate, time of individual treatment, interval between treatments, over-all time of treatment. From the physicist's point of view in the use of beam therapy—the direction of the beam, the combination of multiple ports of entry, and the spatial distribution of radiation are some of the problems. Limitations imposed by the maximum tolerance of the skin, the anatomical configuration of the part traversed by the beam and the position of the lesion are so many added difficulties. To overcome these practical difficulties and to ensure an optimum arrangement for the fields in each individual case, H. T. Flint and C. W. Wilson have constructed suitable frameworks or "jigs" for the various parts of the neck which provide the position of the fields and the direction of the beam. Wilson has thus contributed the principle and provided the facilities for *placing the patient within a known field of radiation in preference to providing unknown fields within the patient.*

Using the present model of the 4 gramme radium unit at Westminster Hospital it takes four to six weeks to treat a lesion in the pharyngeal portion of the tongue; two treatments of fifty minutes each are given daily five days a week. The average tissue dosage is between 5,000-6,000 r; the skin reactions are still at times severe, in degree up to desquamation and moist peeling.

Treatment of cervical lymph nodes.—No method of irradiation can so far compare in adequacy with the surgical removal of the cervical lymph nodes. The wide dissection or "block" dissection associated with the names of Butlin, Crile and, later, Roux-Berger still remains the most certain method of treatment.

The operation should consist in the removal of the deep cervical fascia from the level of the mandible to the clavicle; the sternomastoid muscle, the internal jugular vein, the anterior belly of the omohyoid and often the posterior belly of the digastric are removed, together with the glands in the anterior and submaxillary triangles. It is an operation for the skilled surgeon, and in such hands presents no great risk. The indications for this operation are quite clear-cut: (1) The primary lesion in the tongue should be healed and there must be a reasonable prospect of permanent regression. (2) The glands although palpable and clinically malignant should be mobile or only slightly adherent; they must be not only "removable" but strictly operable. (3) The general health of the patient should not be such as to preclude a major operation. It is necessary to emphasize that the operation should not be undertaken unless these conditions prevail. Incomplete removal is doomed to failure.

If a block dissection is deemed unsuitable, irradiation by teleradium and X-rays is the second-best available. In a few cases additional local needling of a gland or mass is indicated. Regression of cervical lymph nodes for periods of two or three years has been obtained by radiation.

I would have liked to finish this introductory paper with up-to-date statistical tables showing results, but my absence on war service for six and a half years has left a gap in the statistics. The following tables show a record of cases treated before 1939 and a minimum of a five-year survival.

Conclusion.—It is clear that treatment of cancer of the tongue to-day is manifold: radiotherapist, surgeon, physicist, all three are of paramount importance. Adequate treatment needs expensive apparatus, facilities for all types of radiation —beam, needles, seeds, X-rays, laboratories and workshops for the physicists.

that multiplicity of apparently separate primary growths is no bar to radiotherapy; that the actual site influences the technique but not the principles guiding the treatment.

Technique of surgical treatment.—It is the topographically extralingual spread of the disease in certain definite directions which requires extensive and complex treatment. The principles underlying the surgical treatment of such cases are as follows: (1) Control of bleeding should be obtained by preliminary ligation of the lingual arteries or external carotids. Bilateral ligation is sometimes indicated. (2) All intra-oral ablation should be carried out with the diathermy needle, slowly and bloodlessly. (3) Access to the mandible and floor of the mouth should be by reflexion of a flap consisting of the lower lip and the skin of the chin down to the submental area, and extending to the posterior edge of the masseter. (4) The mucosa and the skin should be sutured separately, and drained adequately. With modern methods of anæsthesia, attention to surgical detail and the help of chemotherapy, these operations of considerable magnitude can be carried out with a negligible operative mortality, remarkably little post-operative inconvenience and a speedy recovery.

Age is no contra-indication for such operations. My oldest patient was 76 years of age and has, so far, survived three years without a recurrence.

Cases suitable for surgical treatment are few, no more than 6-7% of cases seen. In the past three years I have had the opportunity of carrying out these operations ten times. There has been so far no operative mortality. 8 of the 10 patients remain free from disease, and 2 died of recurrence; 3 patients were women.

I have come to the conclusion that palliative irradiation of carcinoma of the tongue in cases unsuitable for irradiation is not worth doing as it does not prolong life and rarely increases the patient's comfort. Much better palliation can be obtained by diathermy coagulation.

Radium therapy.—Two methods of radium therapy are employed at Westminster Hospital for cancer of the tongue. Their choice depends solely on the site of the lesion.

For lesions of the anterior part of the tongue insertion of *radium needles* is the method of choice. In lesions of the vallecula, epiglottis, glosso-palatine folds, or in the posterolateral group spreading to the alveolar mucosa or palate, *teleradium* is used. X-ray therapy as the sole method of treatment in cancer of the tongue is disappointing although as an additional source of radiation in cases treated by teleradium, it has proved useful. In both types of cases and in superficial lesions of the floor of the mouth or palate, intra-oral plaques (moulds) are occasionally used to supplement needling or teleradium; especially in cases where, at the junction of the tongue and upper or lower alveolus or the palate, uniform distribution of radiation and an adequate dose are difficult or impossible to achieve by other means.

Distribution of radiation and dosage.—To obtain a homogeneous distribution of radiation in the lesion and surrounding tissue, to assess the quantity of radium needed, and to determine the dose from a given arrangement of needles, the co-operation of a clinically trained physicist is a primary essential. Without such co-operation radium therapy is empirical and there is no control over the efficacy of the radiation. The dosage rate, the total time of treatment, and the estimation of degree of reaction are the clinician's responsibility, and as in other branches of medicine, experience can only be gained by constant practice. The actual insertion of needles or seeds and their retention in the tissues for the desired time require a certain degree of surgical skill. The treatment must be planned and systematic. The lesion in the tongue is of course carefully examined and its extent, position, shape and volume ascertained. The spatial distribution of the needles must fulfil certain physical desiderata and the dosage system devised by Paterson and Parker

first for surface applications, and subsequently worked out by them for interstitial therapy, remains the simplest, the most useful and generally accepted method. As regards the total dose it has varied in our cases from 6,000 r to 9,000 r delivered in 168 hours; the dosage rate showed an equally wide range from 30-75 r/hr. For interstitial treatment an average of six days is now used.

As regards teleradium, a vast amount of clinical, physical and biological research has been done in the past fifteen years. The magnitude of the task can be illustrated by the problems which the treatment presents: total dose, dosage rate, time of individual treatment, interval between treatments, over-all time of treatment. From the physicist's point of view in the use of beam therapy—the direction of the beam, the combination of multiple ports of entry, and the spatial distribution of radiation are some of the problems. Limitations imposed by the maximum tolerance of the skin, the anatomical configuration of the part traversed by the beam and the position of the lesion are so many added difficulties. To overcome these practical difficulties and to ensure an optimum arrangement for the fields in each individual case, H. T. Flint and C. W. Wilson have constructed suitable frameworks or "jigs" for the various parts of the neck which provide the position of the fields and the direction of the beam. Wilson has thus contributed the principle and provided the facilities for *placing the patient within a known field of radiation in preference to providing unknown fields within the patient.*

Using the present model of the 4 gramme radium unit at Westminster Hospital it takes four to six weeks to treat a lesion in the pharyngeal portion of the tongue; two treatments of fifty minutes each are given daily five days a week. The average tissue dosage is between 5,000-6,000 r; the skin reactions are still at times severe, in degree up to desquamation and moist peeling.

Treatment of cervical lymph nodes.—No method of irradiation can so far compare in adequacy with the surgical removal of the cervical lymph nodes. The wide dissection or "block" dissection associated with the names of Butlin, Crile and, later, Roux-Berger still remains the most certain method of treatment.

The operation should consist in the removal of the deep cervical fascia from the level of the mandible to the clavicle; the sternomastoid muscle, the internal jugular vein, the anterior belly of the omohyoid and often the posterior belly of the digastric are removed, together with the glands in the anterior and submaxillary triangles. It is an operation for the skilled surgeon, and in such hands presents no great risk. The indications for this operation are quite clear-cut: (1) The primary lesion in the tongue should be healed and there must be a reasonable prospect of permanent regression. (2) The glands although palpable and clinically malignant should be mobile or only slightly adherent; they must be not only "removable" but strictly operable. (3) The general health of the patient should not be such as to preclude a major operation. It is necessary to emphasize that the operation should not be undertaken unless these conditions prevail. Incomplete removal is doomed to failure.

If a block dissection is deemed unsuitable, irradiation by teleradium and X-rays is the second-best available. In a few cases additional local needling of a gland or mass is indicated. Regression of cervical lymph nodes for periods of two or three years has been obtained by radiation.

I would have liked to finish this introductory paper with up-to-date statistical tables showing results, but my absence on war service for six and a half years has left a gap in the statistics. The following tables show a record of cases treated before 1939 and a minimum of a five-year survival.

Conclusion.—It is clear that treatment of cancer of the tongue to-day is manifold: radiotherapist, surgeon, physicist, all three are of paramount importance. Adequate treatment needs expensive apparatus, facilities for all types of radiation —beam, needles, seeds, X-rays, laboratories and workshops for the physicists.

that multiplicity of apparently separate primary growths is no bar to radiotherapy; that the actual site influences the technique but not the principles guiding the treatment.

Technique of surgical treatment.—It is the topographically extralingual spread of the disease in certain definite directions which requires extensive and complex treatment. The principles underlying the surgical treatment of such cases are as follows: (1) Control of bleeding should be obtained by preliminary ligation of the lingual arteries or external carotids. Bilateral ligation is sometimes indicated. (2) All intra-oral ablation should be carried out with the diathermy needle, slowly and bloodlessly. (3) Access to the mandible and floor of the mouth should be by reflexion of a flap consisting of the lower lip and the skin of the chin down to the submental area, and extending to the posterior edge of the masseter. (4) The mucosa and the skin should be sutured separately, and drained adequately. With modern methods of anæsthesia, attention to surgical detail and the help of chemotherapy, these operations of considerable magnitude can be carried out with a negligible operative mortality, remarkably little post-operative inconvenience and a speedy recovery.

Age is no contra-indication for such operations. My oldest patient was 76 years of age and has, so far, survived three years without a recurrence.

Cases suitable for surgical treatment are few, no more than 6-7% of cases seen. In the past three years I have had the opportunity of carrying out these operations ten times. There has been so far no operative mortality. 8 of the 10 patients remain free from disease, and 2 died of recurrence; 3 patients were women.

I have come to the conclusion that palliative irradiation of carcinoma of the tongue in cases unsuitable for irradiation is not worth doing as it does not prolong life and rarely increases the patient's comfort. Much better palliation can be obtained by diathermy coagulation.

Radium therapy.—Two methods of radium therapy are employed at Westminster Hospital for cancer of the tongue. Their choice depends solely on the site of the lesion.

For lesions of the anterior part of the tongue insertion of *radium needles* is the method of choice. In lesions of the vallecula, epiglottis, glosso-palatine folds, or in the posterolateral group spreading to the alveolar mucosa or palate, *teleradium* is used. X-ray therapy as the sole method of treatment in cancer of the tongue is disappointing although as an additional source of radiation in cases treated by teleradium, it has proved useful. In both types of cases and in superficial lesions of the floor of the mouth or palate, intra-oral plaques (moulds) are occasionally used to supplement needling or teleradium; especially in cases where, at the junction of the tongue and upper or lower alveolus or the palate, uniform distribution of radiation and an adequate dose are difficult or impossible to achieve by other means.

Distribution of radiation and dosage.—To obtain a homogeneous distribution of radiation in the lesion and surrounding tissue, to assess the quantity of radium needed, and to determine the dose from a given arrangement of needles, the co-operation of a clinically trained physicist is a primary essential. Without such co-operation radium therapy is empirical and there is no control over the efficacy of the radiation. The dosage rate, the total time of treatment, and the estimation of degree of reaction are the clinician's responsibility, and as in other branches of medicine, experience can only be gained by constant practice. The actual insertion of needles or seeds and their retention in the tissues for the desired time require a certain degree of surgical skill. The treatment must be planned and systematic. The lesion in the tongue is of course carefully examined and its extent, position, shape and volume ascertained. The spatial distribution of the needles must fulfil certain physical desiderata and the dosage system devised by Paterson and Parker

first for surface applications, and subsequently worked out by them for interstitial therapy, remains the simplest, the most useful and generally accepted method. As regards the total dose it has varied in our cases from 6,000 r to 9,000 r delivered in 168 hours; the dosage rate showed an equally wide range from 30-75 r/hr. For interstitial treatment an average of six days is now used.

As regards teleradium, a vast amount of clinical, physical and biological research has been done in the past fifteen years. The magnitude of the task can be illustrated by the problems which the treatment presents: total dose, dosage rate, time of individual treatment, interval between treatments, over-all time of treatment. From the physicist's point of view in the use of beam therapy—the direction of the beam, the combination of multiple ports of entry, and the spatial distribution of radiation are some of the problems. Limitations imposed by the maximum tolerance of the skin, the anatomical configuration of the part traversed by the beam and the position of the lesion are so many added difficulties. To overcome these practical difficulties and to ensure an optimum arrangement for the fields in each individual case, H. T. Flint and C. W. Wilson have constructed suitable frameworks or "jigs" for the various parts of the neck which provide the position of the fields and the direction of the beam. Wilson has thus contributed the principle and provided the facilities for *placing the patient within a known field of radiation in preference to providing unknown fields within the patient.*

Using the present model of the 4 gramme radium unit at Westminster Hospital it takes four to six weeks to treat a lesion in the pharyngeal portion of the tongue; two treatments of fifty minutes each are given daily five days a week. The average tissue dosage is between 5,000-6,000 r; the skin reactions are still at times severe, in degree up to desquamation and moist peeling.

Treatment of cervical lymph nodes.—No method of irradiation can so far compare in adequacy with the surgical removal of the cervical lymph nodes. The wide dissection or "block" dissection associated with the names of Butlin, Crile and, later, Roux-Berger still remains the most certain method of treatment.

The operation should consist in the removal of the deep cervical fascia from the level of the mandible to the clavicle; the sternomastoid muscle, the internal jugular vein, the anterior belly of the omohyoid and often the posterior belly of the digastric are removed, together with the glands in the anterior and submaxillary triangles. It is an operation for the skilled surgeon, and in such hands presents no great risk. The indications for this operation are quite clear-cut: (1) The primary lesion in the tongue should be healed and there must be a reasonable prospect of permanent regression. (2) The glands although palpable and clinically malignant should be mobile or only slightly adherent; they must be not only "removable" but strictly operable. (3) The general health of the patient should not be such as to preclude a major operation. It is necessary to emphasize that the operation should not be undertaken unless these conditions prevail. Incomplete removal is doomed to failure.

If a block dissection is deemed unsuitable, irradiation by teleradium and X-rays is the second-best available. In a few cases additional local needling of a gland or mass is indicated. Regression of cervical lymph nodes for periods of two or three years has been obtained by radiation.

I would have liked to finish this introductory paper with up-to-date statistical tables showing results, but my absence on war service for six and a half years has left a gap in the statistics. The following tables show a record of cases treated before 1939 and a minimum of a five-year survival.

Conclusion.—It is clear that treatment of cancer of the tongue to-day is manifold: radiotherapist, surgeon, physicist, all three are of paramount importance. Adequate treatment needs expensive apparatus, facilities for all types of radiation—beam, needles, seeds, X-rays, laboratories and workshops for the physicists.

that multiplicity of apparently separate primary growths is no bar to radiotherapy; that the actual site influences the technique but not the principles guiding the treatment.

Technique of surgical treatment.—It is the topographically extralingual spread of the disease in certain definite directions which requires extensive and complex treatment. The principles underlying the surgical treatment of such cases are as follows: (1) Control of bleeding should be obtained by preliminary ligation of the lingual arteries or external carotids. Bilateral ligation is sometimes indicated. (2) All intra-oral ablation should be carried out with the diathermy needle, slowly and bloodlessly. (3) Access to the mandible and floor of the mouth should be by reflexion of a flap consisting of the lower lip and the skin of the chin down to the submental area, and extending to the posterior edge of the masseter. (4) The mucosa and the skin should be sutured separately, and drained adequately. With modern methods of anæsthesia, attention to surgical detail and the help of chemotherapy, these operations of considerable magnitude can be carried out with a negligible operative mortality, remarkably little post-operative inconvenience and a speedy recovery.

Age is no contra-indication for such operations. My oldest patient was 76 years of age and has, so far, survived three years without a recurrence.

Cases suitable for surgical treatment are few, no more than 6-7% of cases seen. In the past three years I have had the opportunity of carrying out these operations ten times. There has been so far no operative mortality. 8 of the 10 patients remain free from disease, and 2 died of recurrence; 3 patients were women.

I have come to the conclusion that palliative irradiation of carcinoma of the tongue in cases unsuitable for irradiation is not worth doing as it does not prolong life and rarely increases the patient's comfort. Much better palliation can be obtained by diathermy coagulation.

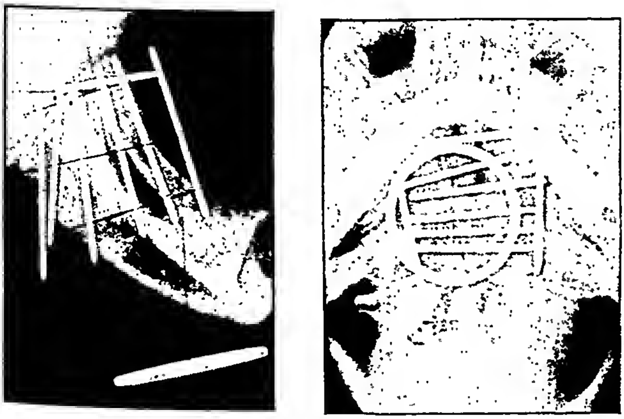
Radium therapy.—Two methods of radium therapy are employed at Westminster Hospital for cancer of the tongue. Their choice depends solely on the site of the lesion.

For lesions of the anterior part of the tongue insertion of *radium needles* is the method of choice. In lesions of the vallecula, epiglottis, glosso-palatine folds, or in the posterolateral group spreading to the alveolar mucosa or palate, *teleradium* is used. X-ray therapy as the sole method of treatment in cancer of the tongue is disappointing although as an additional source of radiation in cases treated by teleradium, it has proved useful. In both types of cases and in superficial lesions of the floor of the mouth or palate, intra-oral plaques (moulds) are occasionally used to supplement needling or teleradium; especially in cases where, at the junction of the tongue and upper or lower alveolus or the palate, uniform distribution of radiation and an adequate dose are difficult or impossible to aehieve by other means.

Distribution of radiation and dosage.—To obtain a homogeneous distribution of radiation in the lesion and surrounding tissue, to assess the quantity of radium needed, and to determine the dose from a given arrangement of needles, the co-operation of a clinically trained physicist is a primary essential. Without such co-operation radium therapy is empirical and there is no control over the efficacy of the radiation. The dosage rate, the total time of treatment, and the estimation of degree of reaction are the clinician's responsibility, and as in other branches of medicine, experience can only be gained by constant practice. The actual insertion of needles or seeds and their retention in the tissues for the desired time require a certain degree of surgical skill. The treatment must be planned and systematic. The lesion in the tongue is of course carefully examined and its extent, position, shape and volume ascertained. The spatial distribution of the needles must fulfil certain physical desiderata and the dosage system devised by Paterson and Parker

case to carry out a careful pre-calculation of any proposed implant so as to bring treatment time as near as possible to the desired over-all time. Even so, however, measurement of exact dimensions on the operating table is far from accurate, so each case is radiographed after implantation. From these radiographs the final estimation of dimensions is made, and hence of the time to give a desired dose. The ring shown on some of the figures is used as a magnification index.

A really poor implant should be dismantled at once and reinserted at a later date. It is indeed one of the defects of permanent radon seed implant that dose cannot be adjusted by alteration of time as with needle implant. Seeds thus call for a much higher degree of accuracy of technique than the needle implant.



A, Side of tongue. B, Dorsum of tongue.

FIG. 1.—Single plane implants.

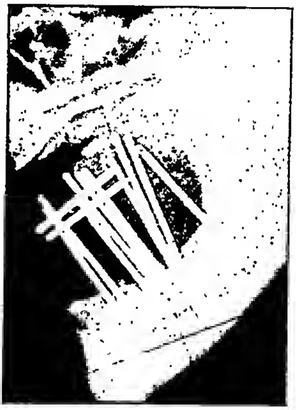
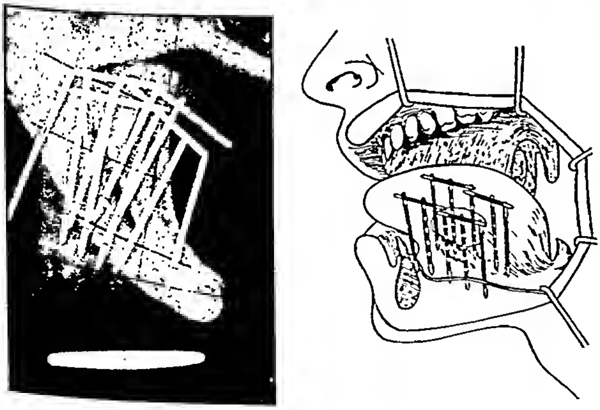


FIG. 3.—Volume implant.



A, Radiograph. B, Diagram.

FIG. 2.—Two-plane implant.

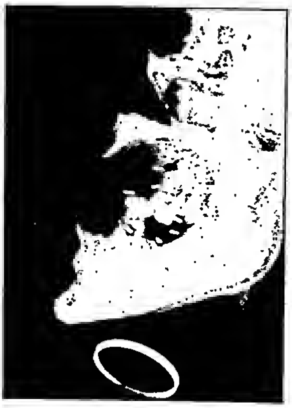


FIG. 4.—Gold seed implant—extensive implant of side of tongue.

It is remarkable how little disturbance most patients suffer even after extensive implants, apart from a rather miserable first post-operative day. Penicillin as irrigation or in lozenges has certainly proved a very great asset in the nursing of mouth cases.

One most important factor requiring further study in relation to satisfactory application of this method of treatment is the dose to be given. There is very little margin between optimum and either insufficient dose or overdosage. In Manchester we have for some time adopted as the standard dose for moderate sized

TABLE I.—CARCINOMA OF TONGUE AND MOUTH. RESULTS OF TREATMENT.

Total treated 1925-37	Site	Total treated for 5 years or more	Net 5-year survival free from disease	%
288	Tongue	213	48	22·6
45	Floor of the mouth	24	10	41·7
12	Alveolar mucosa	6	1	16·7
34	Buccal mucosa	18	11	61·0
30	Hard palate	13	7	53·8
37	Soft palate	20	1	5·0
446	Total	294	78	26·5

TABLE II.—CARCINOMA OF TONGUE 1924-1939. RESULTS IN VARIOUS STAGES.

	Total	Alive: 5 years free of disease	%
	220	49	22·3
Early cases	30	17	56·6
Without glands	60	20	33·3
With glands	130	12	9·2
Site			
Anterior	24	5	20·8
Posterior	89	16	17·9
Inferior	37	8	21·6
Lateral	70	20	28·6

Dr. Ralston Paterson: There are four practical methods of treatment for cancer of the tongue: (1) Radical operations, such as glossectomy and hemi-glossectomy. (2) Electro-coagulation. (3) Radium beam therapy. (4) Radium implant.

The main theme of my contribution is the superiority of radium implant over any of the other methods. This presumes, however, its use as a well thought out technique using a dosage system with post-implantation check by radiograph.

In making such a claim for implant there is no intention of suggesting that the other three methods cannot give results. All of them can yield a percentage of cure; but it is my firm belief that the patient's chance of survival is greatest when implant is the first treatment used. I would place second, radium beam therapy, third, systematic radical operations whose main defect is the mutilation produced, and well down the scale, diathermy, which often proves little more than a snare and a delusion.

It is essential to keep in mind, however, that where irradiation methods fail, as they do in a fraction of cases, the patient can often be given the best second chance by well conceived and well carried out radical surgery.

The first principle of radium implantation is that the implant must approximate to some simple geometrical form to allow measurable dosage. In practice one finds that the available implants fall fairly clearly into four main groups: Single Plane, Two-Plane, Volume, Radon Seeds.

The *single plane* (fig. 1 A and B) may be considered as a palisade of radium which irradiates a slab of tissue from 1-1½ cm. thick. Ideally both ends of this palisade should be crossed, but in practice only the upper end can usually be crossed and allowance is made in the calculation for the open lower end.

The *two-plane* (fig. 2 A and B) consists of two such palisades, parallel to each other, and so planned as to irradiate a somewhat thicker slab of tissue. The irradiated block of tissue, however, is still relatively flat.

Perhaps the most generally applicable implant in tongue is that known as the *volume implant* (fig. 3) in which any roughly spherical tumour can be included within a cylindrical volume of tissue.

There are, however, in the tongue a few sites which do not lend themselves easily to systematic needle implantation—for example lesions of the tip or of the edge of the tongue. For such cases *radon seed implant* (fig. 4) often offers the ideal solution. In a sense this may be regarded as a curved single plane.

Following the general principles first set out by Regaud at the Fondation Curie, these implants should be left in for seven to eight days. It is essential in

TABLE III.—CARCINOMA MOUTH—TONGUE.
Treated by Radium 1932-1938.

	Number treated	5-year survival
Stages I and II—i.e. node-free when first seen	291	41%
Stages III and IV—i.e. nodes present when first seen ..	174	8%
Evaluation of primary treatment taken alone	138	63%

Mr. W. R. Douglas: In this discussion, as a surgeon, I am concerned solely with the treatment of the metastatic cervical field. The emphasis is on the eradication by surgical dissection of the area of the neck likely to be involved and accessible to surgery—in other words, block dissection of the neck.

I shall confine myself to a consideration of block dissection giving the end-results of a series of blocks carried out for tongue primaries. Out of a series of 500 blocks carried out during the last twenty years for varying primaries I have taken from the years 1935 to 1940 a group of 44 cases. This group consists of block dissections carried out for tongue primaries only. Only cases have been included in which both the primary and the glands were proved positive. All others have been eliminated, for, in order to obtain a true estimate of the value of the block in tongue cases, no questionable cases should be included.

The background of the work is important. At the Christie Hospital and Holt Radium Institute in Manchester (a single hospital) we have been able to centralize tongue cases from the peripheral hospitals. This makes for numbers and efficiency. Also all cases are considered by a team, and this combination of surgeon and therapist is, in my opinion, essential. The two are interdependent. Further, there is an intensive annotation and follow-up system, which makes the notes of the cases accurate as far as possible, and invaluable.

In considering the surgical operation of "block neck" one must think in terms of lymphatic field rather than of glands. Metastatic deposits of carcinoma are present not only in the glands, but also in permeated lymphatics spreading from gland to gland. The conception of removal of glands is wrong, it must be a conception of the quadrate sheet of lymphatic tissue carrying the glands.

This lymphatic sheet, with its focal glands, offers marked resistance to systemic spread. No stronger barrier exists in the rest of the body. Systemic invasion is found in only 25% of cases. On this fact, so long as the primary is under control, depends the success of the block operation.

Embolism is erratic, probably dependent on the histological type of the primary, the position in the tongue, the traumatism and movements of the tongue muscles in the region of the growth. Some emboli are notoriously slow in growth in glands, and some rapid—in fact, even with the closest follow-up, they occasionally overtake one. Sometimes emboli, like the afferent lymphatics to a gland, bypass the regional glands and affect glands at a distance. Very occasionally the contralateral glands are involved first.

This erratic distribution stresses the importance of a wide removal.

In considering the cervical field there are four distinct clinical groups:

Group I.—An early primary with no palpable glands. A group which is likely to be controlled easily, and where only about 10% develop glands subsequently. A close follow-up is necessary.

Group II.—An infiltrating growth, with no palpable glands; but where glands develop to the extent of 35% after the primary has been controlled. The vexed question arises as to whether these cases should be blocked, though no glands are palpable—in other words, should a prophylactic block (so-called) be done? From 1932 to 1934 I carried out a series of prophylactic blocks. 18% contained metastatic glands. In the rest, i.e. 82%, no metastatic tissue was found after careful pathological search. I was therefore blocking 4 out of 5 cases needlessly, and subjecting them to a mortality rate of 3%. Moreover, in the 18% which were implants in good tissue 7,000 r over seven days. This dose has to be adjusted downwards with rather larger volumes or where time is found to come appreciably under seven days. It should correspondingly be increased for very small volumes or for relatively extended times. There is some suggestive evidence in an analysis of the treated cases that slight prolongation of the over-all time—for the standard dose of 7,000 r—might be of real value.

If the tongue is to be treated by intra-oral radium, an implant technique is almost always called for. It seems, therefore, desirable to remind you that in the rather wider field of mouth cancer as a whole, a greater variety of techniques is available. Of these the best—ideal where applicable—is the intra-oral radium applicator, so-called dental mould. In the old days we attempted the use of moulds, even for tongue lesions, but it is too mobile an organ and the experiment was a failure. For lesions of the very posterior part of the mouth, including the real base of the tongue just above the vallecula, some method of external radiotherapy, either by radium beam or beam-directed X-rays, is often the treatment of choice.

I have confined myself here to the question of treatment of the primary growth. The secondary gland involvement is important but is a separate theme. It is not too much to say that systematic radical block dissection is an essential part of any mouth cancer treatment policy. Radiotherapeutic methods of dealing with secondary lymph nodes are largely palliative, and do not compete with block dissection.

In matters of this kind results of treatment are inevitably of interest. We can most usefully take as starting point the first table in the Bradshaw lecture given by Sir Alfred Webb-Johnson, *see Brit. med. J.*, 1941 (i), 1 and 39. In this table he contrasts Butlin's original results with those of the Christie Hospital, Manchester, on a group of 1932-1933 cases. He arrives, from these figures, at a decision just slightly in favour of implant.

The figures for the work done after 1933 are, therefore, of interest (*see* Second Statistical Report from the Holt Radium Institute, Manchester, 1934-1938, Livingstone). Table I shows figures for the summated results of the whole period 1932-1938 for cases of cancer of the tongue only, assessed at five years. Of these years, however, 1938 proved itself clearly superior to the others. It is impossible to say whether this improvement, which was considerable, was due to improving technique or was just a vintage year by chance. In the stresses and strains of war organization, we have not been able to repeat these figures although the 1932-1938 over-all standards have been easily maintained. The results of the 1938 work are shown in Table II. The *over-all* inclusive figure of 39% can reasonably be compared with Butlin's figure for *treated cases only* of 27·9%.

Over-all figures, however, only give the one aspect of the picture, so in Table III an effort is made to arrive at some evaluation of the results of treatment of the mouth lesion, as such, disentangled from the effect of lymph-node invasion. The last group of cases includes all cases in the total sample in which the end-result was not determined in any way by the question of secondary node involvement. 63% five-year survival probably does genuinely represent the real value of tongue implant.

TABLE I.—
CARCINOMA MOUTH—TONGUE.
Treated by Radium 1932-1938.

Stage	Number treated	5-year survival
I	146	51%
II	145	31%
III	122	11%
IV	52	2%
Total	465	28%

TABLE II—
CARCINOMA MOUTH—TONGUE.
Treated by Radium 1938.

Stage	Number treated	5-year survival
I	15	71%
II	20	32%
III	10	20%
IV	6	17%
Total	51	39%

moment, provided both ends are found and ligatured. There appears to be an efficient collateral lymphatic circulation.

Patients are shocked for twenty-four hours, but quickly recover. They are up within a week, and go out in ten to fourteen days. Some brawny œdema of the face and neck remains for three to six months. Lip movements at the angle of the mouth are interfered with, usually because of damage to the mandibular branch of the facial nerve. Also, arm movements are somewhat limited, because of trapezius loss, but quite a number of patients go back to work.

Bilateral blocks are carried out with an interval gap between the two sides of not less than three weeks, leaving the second internal jugular. Both internal jugulars can be safely taken if there is a three-months' interval. Cases have been done with a shorter interval, but it is wiser to allow a venous collateral circulation to be properly established.

End-results.—In estimating the results of block necks for tongue primaries, no attempt has been made to differentiate between anterior and posterior lesions, or between early and borderline cases. All are included. The five-year survival rate, in which cases are well, with no clinical sign of secondaries, is 30% of all the cases blocked for tongue carcinoma.

Lieut.-Colonel W. L. Harnett (*Medical Secretary to the Clinical Cancer Research Committee of the British Empire Campaign*) said that he had the permission of the Committee to bring forward statistics of 287 cases of cancer of the tongue collected from all the London hospitals between April 1, 1938, and September 3, 1939. These cases constituted 1·9% of all the cancer cases registered, corresponding closely to the Registrar-General's figure of 1·7% for England and Wales in 1937. There were 247 males and 40 females, a ratio of 6 to 1.

The cases were grouped as follows:

	Number		%
Stage I—Confined to organ of origin	101		35·2
Stage II—Adjacent tissues invaded, but lymph nodes not involved ..	21		7·3
Stage III—Lymph nodes involved :			
(*a*) Adjacent tissues not invaded	95	162	56·4
(*b*) Adjacent tissues invaded	67		
Stage IV—Remote metastases present	3		1·0

There were also 65 cases of carcinoma of the vallecula and epiglottis, which had been included with growths of the pharynx.

TABLE I

The grouping and methods of treatment used in the various stages and the results were:—

	Number	Survived 5 years	Died with cancer	Died without cancer	Untraced
Stage I—					
Anterior site, 90					
Posterior site, 11					
Surgical or diath. excision ..	32	12	15	4	1
Interstitial radium	26	9	16	1	—
Teleradium	11	1	10	—	—
High-voltage X-rays	11	2	7	1	1
Excision and interstitial radium..	9	5	4	—	—
Combined radium and X-rays ..	10	2	8	—	—
Not treated	2	—	2	—	—
Survival rate=30·7%	101	31	62	6	2
Stage II—					
Anterior site, 13					
Posterior site, 8					
Surgical or diath. excision ..	2	1	1	—	—
Interstitial radium	4	—	3	1	—
Teleradium	5	3	1	1	—
X-rays alone or with radium ..	8	1	6	1	—
Not treated	2	—	2	—	—
Survival rate=23·8%	21	5	13	3	—

blocked, the results were little, if any, better than if we had waited for glands to appear. We now adopt a "watch technique" and wait for glands to be palpable. Then a block is carried out, the optimum time being at least six weeks after the primary has settled, so as to avoid the reaction phase. 60% of cancer clinics throughout the world adopt the "watch technique" but it is dangerous unless a close intensive follow-up is observed. If the patient is likely to live abroad, or is non-co-operative, it is better to carry out a prophylactic block; if the lesion is unilateral, then a unilateral block; if a mid-line lesion, then a bilateral block, with an interval of at least three weeks between the two sides.

Group III.—An infiltrating growth, often advanced, with palpable glands. The majority of cases present themselves in this stage for the first time. If the glands are early and are blockable, wait until the primary has been treated and has reacted before carrying out the block. If glands are fixing and are borderline, then fine judgment is required as to whether and when to block. Fixation does not necessarily mean extracapsular spread. It may be only inflammatory, due to sepsis in the primary growth. Borderline cases, if at all possible, should be given a chance. Either treat the primary with gold seed implant or diathermy, and block at the same time; or, if external radiation is used, then block the day after radiation treatment (assuming a one-day intensive treatment is given). Do not wait for the reaction. Flaps are apt to necrose and sepsis to supervene, if the block is done during the reaction phase.

Group IV.—Advanced cases, in which the glands are inoperable and fixed. If the primary can be controlled—and this, of course, cannot be foretold, especially in advanced cases—occasionally it is possible by external radiation to bring an apparently inoperable mass to a stage when it is operable, by reducing the size and the fixity, but these are desperate cases, and only occasionally can one be salvaged.

Three types of operation are in use: (1) The suprahyoid block. (2) The supra-omohyoid block. (3) The full radical block, founded on the Crile block operation of forty years ago. All may be unilateral or bilateral.

The first two types of operation are partial block operations, and consist chiefly in dissection of glands. They are in my considered opinion incomplete, and therefore dangerous. The supra-omohyoid operation takes in a wider sweep than the suprahyoid in that it includes a dissection of the upper deep cervical glands, but any gland dissection is an operation to be avoided.

The radical block is the operation of choice. The cases are usually males, in the proportion of ten to one female, in the region of 60 years old, often in poor general condition because of pain and difficulty in feeding. Arteriosclerosis and chest complaints are common. Yet, in spite of these disabilities, it is remarkable how well they stand up to a full block. Complications are few, and the mortality is 3%. In the last 50 cases our mortality has been nil. It is therefore as safe a procedure as a radical mastectomy.

The anæsthetic we use is pentothal-intratracheal gas and oxygen with a minimum of chloroform. The skin flaps do not include the platysma. The block of tissue is turned back from the mid-line to the trapezius as a hinge. The block includes digastric (both bellies), the omohyoid and the sternomastoid. The spinal accessory is cut across at the level of the transverse process of the atlas, and at this level the internal jugular is double-ligatured.

The block of tissue is freed from carotid and vagus, and all the small cross veins (pharyngeal, facial and thyroid) tied, before the internal jugular is double-ligatured above and below. The second, third and fourth cervical nerves are cut across as the block of tissue is carried back. The fascia is stripped clean from splenius and levator anguli muscles. Any attempt to preserve spinal accessory and cervical nerves interferes with a clean dissection, and therefore might affect the end-result. On the left side the thoracic duct may be injured. This is of no

Section of Ophthalmology

President—HAROLD LEVY, F.R.C.S.

December 13, 1946]

MEETING HELD AT MANCHESTER ROYAL EYE HOSPITAL

Isolated Oculomotor Palsy Caused by Intracranial Aneurysm

By GEOFFREY JEFFERSON, C.B.E., M.S., F.R.S.

ABSTRACT.—The present paper is concerned with the 55 aneurysms out of a total of 158 that caused isolated paralysis of the oculomotor nerve. The majority arose from the internal carotid artery after it had pierced the dura (supraclinoid). Rarely the aneurysm sprang from the basilar artery. In two-thirds of the cases there had been a subarachnoid hæmorrhage from leakage. Not more than 10% of patients had arteriosclerosis. Calcification of the sac is not a sign that the aneurysm has thrombosed. The only certain way of demonstrating the position and size of an intracranial aneurysm is by arteriography, which is a safe procedure.

The correct treatment is by carotid ligature. In about 8% of normals the circle of Willis is incomplete, therefore percutaneous compression must first be tried. The only fatalities from ligature were in persons in the acute stage of subarachnoid hæmorrhage. Such cases died because of intracerebral hæmorrhage, not from meningeal bleeding alone. In this type of case a clip applied to the neck of the sac is probably a better method. In the more usual cases where the hæmorrhage has been spontaneously arrested common carotid ligature in the neck is probably a little safer than intracranial clipping.

RÉSUMÉ.—Sur 158 anévrysmes, 55 ont donné lieu à une paralysie isolée du nerf oculomoteur. Il s'agit ici de ces 55 cas. Le plus souvent ces anévrysmes sont situés sur la carotide interne au-dessus de sa perforation de la dure-mère (supra-clinoïde), et très rarement sur l'artère basilaire. Deux tiers des cas avaient eu une hémorragie sous-arachnoïdienne par fissure de l'anévrysme. Seulement 10 pour cent des malades souffraient d'artériosclérose. La calcification du sac n'est pas un signe de thrombose de l'anévrysme. La localisation et la grosseur de l'anévrysme ne peuvent être montrées avec certitude que par l'artériographie, qui est peu dangereuse.

Le traitement correct est la ligature de la carotide. Le cercle de Willis étant incomplet dans environ 8 pour cent des cas normaux, il est nécessaire d'essayer d'abord la compression percutanée. Les seuls décès après la ligature survinrent chez des malades opérés dans la phase aigüe de l'hémorragie sous-arachnoïdienne. Ces malades sont morts d'une hémorragie intracérébrale, et non pas d'une simple hémorragie méningée. Dans les cas de ce genre il est probablement préférable de poser un clip sur la tige de l'anévrysme. Dans les cas plus ordinaires, où l'hémorragie s'est arrêtée spontanément, il est probablement un peu moins dangereux de lier la carotide primitive que de poser un clip intracranien.

SUMARIO.—En éste trabajo se estudian los 55 aneurismas que, de un total de 158, causaron parálisis aisladas del nervio motor ocular común. La mayoria radicaban en la arteria carótida interna después de su penetración en la duramadre. En casos excepcionales el aneurisma se hallaba asentado en la arteria basilar. En las dos terceras partes de los casos, existia el antecedente de hemorragia subaracnoidea causada por pérdida sanguínea gota á gota. Los enfermos afectos de arterio-esclerosis no excedieron del 10%. La calcificación del saco no presupone que el aneurisma se halle trombosado. El único procedimiento para demostrar la situación y el tamaño del aneurisma intracraneal con certeza, lo proporciona la arteriografía, procedimiento desprovisto de peligro.

Stage III— Anterior site, 98 Posterior site, 56 Whole tongue 8	Number	Survived 5 years	Died with cancer	Died without cancer	Untraced
Surgical or diath. excision	7	—	7	—	—
Interstitial radium	43	5	37	—	1
Teleradium	25	1	23	1	—
High-voltage X-rays	38	2	36	—	—
Excision and radiation	6	—	5	—	1
Combined radium and X-rays	20	2	17	—	1
Not treated	23	—	23	—	—
Survival rate=6·2%	162	10	148	1	3
Stage IV—					
Interstitial radium	1	—	1	—	—
Not treated	2	—	2	—	—
	3	—	3	—	—

A method of estimating the five-year survival rate by comparing the actual survival time in months with the expected survival for five years of a group of the general population having the same age-sex constitution was then explained. Expressing the actual survival time as a percentage of the expected survival, the results of treatment are shown in Table II.

TABLE II

	Number of cases	% of expected Stage I	 Stage III
Surgical or diathermy excision	37	88·4	28·3
Interstitial radium	66	64·1	43·5
Teleradium	33	62·8	32·9
High-voltage X-rays	44	59·7	34·7

The above figures deal only with the treatment of the primary growths.

Mr. Anthony Green: *Radon seed chains for carcinoma of the tongue.*—Two points have been brought out by previous speakers: First, that interstitial radiation gives the best results in treatment of cancer of the tongue, and second that radon seeds are in some instances desirable because of the site and extent of growth and/or the general condition of the patient.

At the Royal Northern Hospital a method of chain radon seed implant has been developed. This has the advantages of a radon seed implant in that an old patient can move his tongue, cough and spit without distress. Moreover many of the advantages of the radium needles are preserved in so far as the distribution of radiation is very much better than with individual radon seeds and that the seed chains can be removed at any time during the treatment. Strong end loading of the seeds saves the necessity of crossing the ends as with radium needles.

The radiographs (not reproduced) show two cases of chain seed implants into the tongue indicating how evenly the distribution can be obtained for the dorsum of the tongue or the lateral surface of the tongue; moreover the flexible nature of these chains makes it possible to irradiate curved surfaces such as the base of the tongue. This method of implantation depends for success on careful and close team-work with physicists.

The seeds are introduced with difficulty by pulling them after a stout needle inserted through the tissues, or better still by inserting them through a trochar and cannula especially made for the purpose.

The results of this new method, which is now between two and three years old, are encouraging, and the King Edward's Hospital Fund for London has financed further investigation and development of this type of treatment for this and other sites in the body.

the internal carotid, middle cerebral and basilar arteries are the commonest sites for aneurysm and are roughly equally vulnerable in this respect. Carotid aneurysms are reasonably easy to diagnose but the basilar are much more difficult, so that the former produce the chief material for clinical, as opposed to pathological, study. This fact is made abundantly clear from the fact that of 143 basilar aneurysms collected by McDonald and Korb, no less than 139 were post-mortem discoveries. Had every case been correctly diagnosed beforehand the result would have been no different, for surgery has no answer to the basilar aneurysm. The case is fortunately quite different with aneurysms of the carotid tree, as my own material shows, for in arteriography, carotid or vertebral, we have a method which shows clearly in most cases the exact site of the aneurysm, a fact of great practical importance.

The congenital nature of the majority of these aneurysms from defects in the muscular coat (Eppinger, 1887; Forbus, 1930) is agreed on all hands, the word "congenital" being used in the same sense as when it is applied to an inguinal hernia appearing in later life. It is unlikely that aneurysms often exist from birth onwards, they develop later through inborn defects. Occasionally they must be truly congenital as in one patient of mine, a baby 9 months old who nearly died of a subarachnoid hæmorrhage and was blind for nearly three weeks from subhyaloid hæmorrhages. She is recovering. This is one of the youngest patients on record.

My own material of 158 cases seems to be the largest in which the patients have been observed during life by one man. Beadles' (1907) famous collection contained 555 cases but 114 came from the post-mortem room and from hospital museums, 441 from the literature; Dandy describes 108 cases in his book, but 44 of them were from the post-mortem register at Johns Hopkins Hospital, the valuable study of McDonald and Korb is entirely a compilation save for 2 cases. My own cases are analysed in Table I. I have not used the necropsy material of the Royal Infirmary unless I had observed the case whilst alive.

TABLE I

A. Subarachnoid hæmorrhages without local signature			32
B. Supraclinoid carotid aneurysms (after the vessel has penetrated the dura) ..			55
C. Carotid aneurysms in cavernous sinus (infraclinoid)			45
	Saccular	spontaneous	27
	„	traumatic	0
	Fistulous	spontaneous	4
	„	traumatic	14
D. Aneurysms compressing the visual pathways (optic nerve, chiasma, tract) ..			19
E. Aneurysms producing neurological signs other than ocular or oculomotor ..			7

This is very much a surgeon's picture because the first group of plain subarachnoid bleeding is relatively small; such cases are usually admitted to medical wards. Of the 32 cases of this kind, 10 died in hospital, 16 are known to be alive and well, 6 are untraced. The lengths of survival have been 13, 12, 12, 11, 7, 7, 5, 4 and less years.

THE ISOLATED OCULOMOTOR PALSIES

That an intracranial aneurysm might cause oculomotor palsy has long been known. Examples can be found in those admirable collections of cases made by Brinton (1851-52), Gull (1859), Peacock (1876), von Hoffmann (1894), Fearnsides (1916), Conway (1926) and Szekely (1928), papers that are amongst the classics of the earlier literature of aneurysm. One of the first, if not the first, to speak specifically of the relationship between oculomotor palsy and aneurysm was France, ophthalmic surgeon to Guy's Hospital. Writing in 1846 he said that given a third nerve palsy with no evidence of tumour we should not be far wrong in assuming that the cause was "a sanguineous effusion of circumscribed vascular enlargement in the vicinity of the nerve of the third pair". He based this opinion on the post-mortem findings in a clinically observed case. This was an inspired deduction but although the fact was there to know it must have been remembered by very few, since the establishment of a real clinical picture of aneurysm as a clinical entity rather than as a museum piece, as something likely to cause signs that could be recognized and traced to a source during life, was left to C. P. Symonds (1923). The relationship between oculomotor palsy and aneurysm was further observed by Albright (1929), Dott (1933), Nattrass (1928), E. Bramwell (1934), Garvey (1934) and by myself in published and unpublished material.

The third nerve leaves the mid-brain from the medial border of the crus cerebri and as Weber long ago pointed out the approximation allows perfectly of a syndrome of crossed

El tratamiento correcto consiste en la ligadura de la arteria carótida. Cerca del 8% de los individuos normales poseen el círculo de Willis incompleto y por ésta razón la compresión transcutánea debe intentarse inicialmente. Los únicos resultados fatales de la ligadura ocurrieron durante el período agudo de la hemorragia subaracnoidea. La causa de la muerte fué, no solo la hemorragia meníngea, sino también la hemorragia intracerebral. En estos casos es probablemente lo mejor aplicar un *clip* al cuello del saco. En casos más frecuentes, en los que la hemorragia ha cesado espontáneamente, la ligadura de la arteria carótida en el cuello es probablemente algo más segura que la aplicación de un *clip* intracraneal.

АБСТРАКТ.—Настоящая статья касается только 55-ти из 158-ти случаев аневризм, которые произвели изолированный паралич глазо-моторного нерва. Большинство аневризм возникло из внутренней сонной артерии после ее прободения через верхне-клиноидную часть твердой оболочки. Реже аневризма возникала из базилярной артерии. В двух третях случаев было субарахноидальное кровотечение вследствие просачивания крови. Не более как 10% больных страдало артериосклерозом. Кальцификация аневризменного мешка не является признаком тромбоза аневризмы. Единственным способом демонстрации позиции и величины интракраниальной аневризмы является артериография, которая представляет из себя совсем безопасную процедуру.

Правильным лечением является лигатура сонной артерии. В 8% артериальный круг Виллиса несовершенный, и оттого необходимо прежде всего испробовать чрезкожное сдавливание артерии. Смертельный исход от лигатуры бывает только в тех случаях, когда имеется острая стадия субарахноидального кровотечения. Такие больные умирали не исключительно от менингиального, а от внутримозгового кровотечения. В таких случаях перевязка шейки аневризменного мешка является лучшим способом. В более обыкновенных случаях, когда кровотечение останавливалось самопроизвольно, лигатура общей сонной артерии на шее более безопасна, чем внутримозговая перевязка.

In my previous writings a beginning was made at systematizing the semiology of aneurysms of the circle of Willis according to dominant symptom-sign patterns. This breaking down of the neurological consequences of aneurysms has always appeared to me to be a major work and a necessary prelude to the growth of knowledge, for it is likely that the prognosis of vascular abnormalities in different situations may well have different significances in terms of working capacity and survival. I propose to carry the matter further by presenting my 55 cases in which an isolated third nerve paralysis has been the essential feature.

This subject is one of great fascination and since many of the clinical syndromes come within the province of the ophthalmologist it should be of interest to present the relative frequency with which they have occurred in so far as illustrations can be drawn from the experience of one man. I have reviewed the literature in my previous papers (1937, 1938). Since then there have been some notable contributions: McDonald and Korb (1939), Richardson and Hyland of Toronto (1941), Krayenbühl of Zürich (1941), and Dandy of Baltimore (1944). The diagram of McDonald and Korb constructed from a review of 1,125 reported cases is so generally informative that it is reproduced here (fig. 1). This shows that

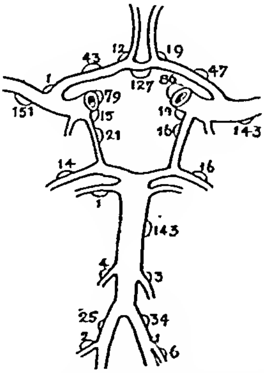


FIG. 1.—Schema of aneurysmal sites in 1,023 (of 1,125) cases.
From McDonald and Korb, *Arch. Neurol. Psychiat., Chicago*, 1939, 42, 298.

the internal carotid, middle cerebral and basilar arteries are the commonest sites for aneurysm and are roughly equally vulnerable in this respect. Carotid aneurysms are reasonably easy to diagnose but the basilar are much more difficult, so that the former produce the chief material for clinical, as opposed to pathological, study. This fact is made abundantly clear from the fact that of 143 basilar aneurysms collected by McDonald and Korb, no less than 139 were post-mortem discoveries. Had every case been correctly diagnosed beforehand the result would have been no different, for surgery has no answer to the basilar aneurysm. The case is fortunately quite different with aneurysms of the carotid tree, as my own material shows, for in arteriography, carotid or vertebral, we have a method which shows clearly in most cases the exact site of the aneurysm, a fact of great practical importance.

The congenital nature of the majority of these aneurysms from defects in the muscular coat (Eppinger, 1887; Forbus, 1930) is agreed on all hands, the word "congenital" being used in the same sense as when it is applied to an inguinal hernia appearing in later life. It is unlikely that aneurysms often exist from birth onwards, they develop later through inborn defects. Occasionally they must be truly congenital as in one patient of mine, a baby 9 months old who nearly died of a subarachnoid hæmorrhage and was blind for nearly three weeks from subhyaloid hæmorrhages. She is recovering. This is one of the youngest patients on record.

My own material of 158 cases seems to be the largest in which the patients have been observed during life by one man. Beadles' (1907) famous collection contained 555 cases but 114 came from the post-mortem room and from hospital museums, 441 from the literature; Dandy describes 108 cases in his book, but 44 of them were from the post-mortem register at Johns Hopkins Hospital, the valuable study of McDonald and Korb is entirely a compilation save for 2 cases. My own cases are analysed in Table I. I have not used the necropsy material of the Royal Infirmary unless I had observed the case whilst alive.

TABLE I

A.	Subarachnoid hæmorrhages without local signature		32
B.	Supraclinoid carotid aneurysms (after the vessel has penetrated the dura)		55
C.	Carotid aneurysms in cavernous sinus (infraclinoid)		45
	Saccular spontaneous	27	
	„ traumatic	0	
	Fistulous spontaneous	4	
	„ traumatic	14	
D.	Aneurysms compressing the visual pathways (optic nerve, chiasma, tract)		19
E.	Aneurysms producing neurological signs other than ocular or oculomotor		7

This is very much a surgeon's picture because the first group of plain subarachnoid bleeding is relatively small; such cases are usually admitted to medical wards. Of the 32 cases of this kind, 10 died in hospital, 16 are known to be alive and well, 6 are untraced. The lengths of survival have been 13, 12, 12, 11, 7, 7, 5, 4 and less years.

THE ISOLATED OCULOMOTOR PALSIES

That an intracranial aneurysm might cause oculomotor palsy has long been known. Examples can be found in those admirable collections of cases made by Brinton (1851-52), Gull (1859), Peacock (1876), von Hoffmann (1894), Fearnsides (1916), Conway (1926) and Szekely (1928), papers that are amongst the classics of the earlier literature of aneurysm. One of the first, if not the first, to speak specifically of the relationship between oculomotor palsy and aneurysm was France, ophthalmic surgeon to Guy's Hospital. Writing in 1846 he said that given a third nerve palsy with no evidence of tumour we should not be far wrong in assuming that the cause was "a sanguineous effusion of circumscribed vascular enlargement in the vicinity of the nerve of the third pair". He based this opinion on the post-mortem findings in a clinically observed case. This was an inspired deduction but although the fact was there to know it must have been remembered by very few, since the establishment of a real clinical picture of aneurysm as a clinical entity rather than as a museum piece, as something likely to cause signs that could be recognized and traced to a source during life, was left to C. P. Symonds (1923). The relationship between oculomotor palsy and aneurysm was further observed by Albright (1929), Dott (1933), Nattrass (1928), E. Bramwell (1934), Garvey (1934) and by myself in published and unpublished material.

The third nerve leaves the mid-brain from the medial border of the crus cerebri and as Weber long ago pointed out the approximation allows perfectly of a syndrome of crossed or alternating hemiplegia. When contralateral limb signs are present they usually indicate a small intracerebral hæmorrhage, rather than crus compression. The latter is a rare happening and aneurysms which affect the nerve do not usually impinge on the crus (*see* Milletti's exceptional case, 1946). The reason is what we might call the "type aneurysm", producing oculomotor palsy alone, is rarely large enough to reach the crus, the nerve being compressed at the anterior end of its course through the basal cisterns and just as it plunges into the dural covering of the cavernous sinus. Reference to fig. 2 will make this clearer; it will be seen that a relatively small aneurysm easily reaches the oculomotor nerve and I have indicated that the nerve is vulnerable to blow-outs on the walls of either the carotid or of one or the other of the vessels that comprise the posterior end of the circle of Willis. In point of fact, the anterior (i.e. carotid) aneurysms of the circle of Willis far outnumber the basilar in causing oculomotor palsy —52 of my 55 cases. It seems rather curious considering the high necropsy incidence of basilar aneurysms that in surgical practice they should so uncommonly compress the third nerve. The deduction that I draw is that, although theoretically (*see* fig. 2) they could produce much the same cranial nerve palsies as do those of carotid origin, they do not. The probability of a third nerve palsy is not in fact great unless the aneurysm springs from the basilar at its bifurcation and the majority occur on the stem more caudally. A fairly large number of basilar aneurysms gives rise to a plain subarachnoid hæmorrhage, the source of the hæmorrhage remaining clinically undecipherable.

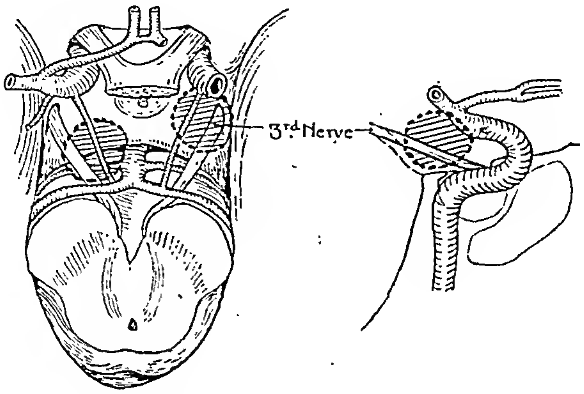


FIG. 2.—Relationship of carotid to third nerve.

A very good example of an average supraclinoid aneurysm is shown in a drawing by that most intelligent and accomplished man, the late Dr. E. W. Twining (fig. 3). The case illus-

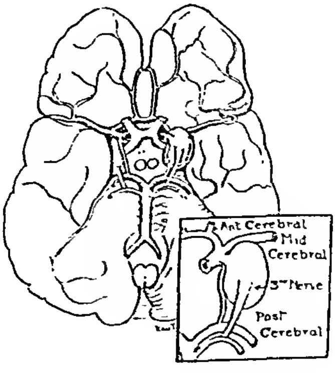


FIG. 3.—Drawing of supraclinoid aneurysm, causing third nerve palsy (E. W. Twining).

trated is of some historical importance since it is the first in which a direct attack was made on an intracranial aneurysm. This was in 1927 and although I failed to accomplish anything it was a first step in the right direction, i.e. verification and cure.

In the illustration the aneurysm can be seen to arise from the carotid trunk soon after it has entered the cranial cavity by piercing the dura. It is, therefore, supraclinoid in position. The posterior communicating artery runs back below the aneurysm, but in another example it might have been above it. The sac is directed backwards and is pear-shaped, two features which are remarkably constant. Eppinger noticed that aneurysmal sacs were usually orientated in the direction of the blood flow but we may be sure that whatever the factors are that rule the configuration of aneurysms, they take their shape, size and direction because they must. In fig. 4 (p. 429) the sacs of aneurysms will be seen delineated in life by arteriography; the aneurysms are small and strikingly similar in shape and situation, all arise from roughly the same point on the carotid. I can see no other explanation for such relative uniformity except (*a*) that the area of vessel wall that gives way is always very limited, probably no more than 2 or 3 mm. in diameter, (*b*) that it is nearly always in the same place, and (*c*) that the aneurysm's eventual size depends on the intravascular pressure and the material available for repair. I fancy that the small extent of the weakened wall is the most important feature.

Referring again to fig. 3 the third nerve is seen to be flattened and to disappear on the sac. The nerve is rarely completely divided by the pressure of the sac, for in all survivors but one it has recovered, though recovery may be long delayed and incomplete. Judged from proven cases in my own series the aneurysm that caused the oculomotor palsy sprang from the carotid in all but three, who had negative carotid angiograms. Presumably in those the site of the aneurysm was the basilar or posterior cerebral in the beginning of its course. Had they come from the posterior communicating artery they would probably have filled with thorotrast; the basilar aneurysm never does so unless the vertebrals are themselves injected.

SIGNS AND SYMPTOMATOLOGY

The most striking feature of any third nerve palsy is, of course, ptosis. The closure of the eye has in every case been preceded by a short period of diplopia and visual confusion which patients have not always correctly analysed subjectively.The sufferers are usually in such severe pain in the ipsilateral forehead and in the eye that they have been in no state for introspection. The majority of the patients localize the pain to the forehead, side of the nose and inner canthus where it is singularly sharp and penetrating; this seems to be a characteristic pain. A constant feature, too, has been the statement that they have closed the lid because it felt heavy and because the pain was so severe that it made them close the eye. They wake one morning, one to seven days after the onset, to find that it will no longer open. It then remains closed for several weeks, but very rarely indeed permanently, whether the carotid is ligatured or not. The cause of the recovery is partly shrinkage by thrombosis sufficient to free the nerve to some extent as a sequel either of ligature or of natural causes. It may be due partly to the action of Müller's muscle. Although considerable recovery takes place in time, the nerve in my experience almost never regains function so completely that there is perfect mobility of the globus oculi in all directions and with parallel visual axes. The movement that returns best is internal rotation; by synergy with the external rectus horizontal movement is good. The muscle that recovers least well is the superior rectus and here is often seen a curious paradox, that the upper lid recovers and is elevated enough to allow of free vision while the superior rectus remains paralysed. The cause is most likely to be found in the action of Müller's muscle: I discussed this important feature of dissociated recovery in my 1938 paper, adopting an explanation by axon crossing in regeneration even although the internal pattern of the nerve is not much disrupted. The same features were observed in experimental division of the third nerve in the macaque by Mahoney and Sheehan (1936). They ascribe the opening of the lid to Müller's muscle. Another curious feature can be observed in downward movement, the lid often elevates a millimetre or so for a fraction of a second as the globe turns down and then the lid descends. L. Rogers (1946) has recently described another feature—opening of the lid on turning the eyes to the opposite side.

The pupil is only at first classically dilated and fixed but within two to four weeks it usually contracts somewhat, though remaining larger than that on the normal side. Occasionally a sluggish light reaction reappears and a parasympathetic reinnervation may be assumed. The reduction of the pupillary aperture as a natural event before the recti recover seems to indicate that the dilator fibres are incapable of maintaining a constant and permanent maximal contracture tonus. The lack of complete recovery in the nerve as a whole may be of the same order as in the severer cases of facial palsy where movement never returns with all the nuances and qualities of the normal. The failure is very likely contributed to by the pressure of the aneurysm, for even should it completely thrombose there will still remain a mass submitting to the pulsations of the carotid artery. That the nerve can escape from it seems impossible.

The pain in the head which is the characteristic and distinguishing accompaniment of aneurysmal compression of the third nerve is unilateral and within the distribution of the first division of the trigeminus. This is a referred pain and must be due to stimulation by the aneurysm of sensitive basal structures. The most likely site for this is the upper border of the cavernous sinus, to which the sac may become adherent. I have found that electrical stimulation at this place under local anæsthesia causes severe pain in the eye and forehead. The only alternative mechanism that suggests itself is that the pain is caused by a drag on the arterial trunk itself, i.e. that the aneurysm's pulsation pulls on the vessel. This is possibly the commoner cause. Either explanation would give the reason why pain ceases when the aneurysm thromboses, for this is the case.

There may be overflow beyond the confines of the ophthalmic trigeminal division when the pain is severe, but violent occipital pain, especially when associated with nuchal stiffness, indicates that the aneurysm is leaking into the subarachnoid spaces. In parenthesis, it may be recollected that it was the pain accompanying the oculomotor palsy that led the older clinicians to diagnose these aneurysmal cases as examples of neuritis of some theoretical sort or another, or of periostitis of the superior orbital fissure. Actual anæsthesia of the first division does not occur with supraclinoid aneurysms. When present it is a sure indication of a subclinoid anterior cavernous aneurysm and usually carries with it paralysis of more motor nerves to the globus oculi than the third alone (Jefferson, 1938).

On the other hand these supraclinoid aneurysms not uncommonly produce a subjective feeling of numbness in the forehead and nose when the pain is very severe though the corneal reflex is not recognizably diminished. This is a puzzling symptom. It might be due to the aneurysm exerting pressure from without on the ophthalmic fibres of the trigeminal nerve as they lie in the roof of the cavernous sinus.

Subarachnoid hæmorrhage: There have been in my series of 55 cases of aneurysmal isolated oculomotor palsy, 40 in which a subarachnoid hæmorrhage has occurred by leakage, i.e. about 70%. In 7 it was so severe as to be fatal whilst the patients were still in hospital but was usually not very bad. The results in the others will be given later, nearly all immediate survivors are still alive (*see* Table of Cases). There is no doubt that the most dangerous period is the initial bleeding, the period of the sufferer's first admission to hospital. If he recovers then his chances are very fair but not perfect. The following cases illustrate these hazards:

CASE I.—A. S., female, aged 21, was admitted to the medical ward of the Royal Infirmary 23.8.27 as an urgency complaining of head pains and diplopia. She had collapsed during her honeymoon with terrific pain in the head and neck, had lost consciousness and remained semiconscious for a week, then slowly recovered. The left eye was found to be closed when she was conscious enough to test it and remained so for four months when it opened with consequent diplopia. The pain was situated in the left forehead low down, at the inner canthus. A year later she was readmitted after an attack of severe pain like a knife entering the left vertex, she lost consciousness for an hour or so and was doubly incontinent. The positive neurological signs were partial left third nerve palsy, dilated fixed left pupil and hæmorrhages into the left disc. She rapidly recovered. She was then lost sight of for eleven years when she was readmitted 30.8.39. She had collapsed in the street from a subarachnoid hæmorrhage. She was transferred from a neighbouring hospital twelve days later; there were still 150,000 red cells in a yellowish cerebrospinal fluid indicating that some leakage from her aneurysm had continued. There were again hæmorrhages in the discs and a complete left oculomotor palsy. There was no trigeminal anæsthesia. She gave a history of several losses of consciousness during the years past; these were epileptic episodes and were no doubt caused by a brain-scar from leakage of blood into brain tissue. Epilepsy is a not uncommon sequel in survivors of aneurysmal hæmorrhages (Jefferson, 1937). X-rays of her skull showed a fine pea-shaped scale of calcification opposite the tip of the left posterior clinoid process. This was evidently the wall of the aneurysm; recent hæmorrhage demonstrated that however impervious the wall might be in its calcified part it was still frangible elsewhere on its circumference. That the weak place was at the neck subsequent events were to show. Arteriograms were made revealing a sizable cavity inside the aneurysm (fig. 4c). I decided to put a silver clip on the neck of the aneurysm. This was done through a transfrontal flap on 14.9.39. After a ventricular tap had removed 25 c.c. of yellow fluid the left frontal lobe was easily elevated. There were dense arachnoidal adhesions about the left optic nerve. The aneurysm was at once visible behind and lateral to the trunk of the carotid artery. It was round and greyish-yellow, measuring about 1·5 cm. across. By gentle dissection and by rotating the aneurysm laterally its neck was well seen. A silver clip was placed upon it but I was not satisfied that it grasped it completely across. A second clip was therefore tightened on the neck. The closure of the clip was followed by an immediate gush of blood that filled the wound in a second or two. Clearly the neck had given way. The bleeding was controlled with hot wet cotton packs held in situ by gentle pressure whilst the anæsthetist compressed the carotid in the neck and Mr. Schorstein cut a muscle graft from the thigh. The cotton packs were removed and the hæmorrhage was found to be arrested. Muscle was tucked in around the aneurysm to form as complete an ensheathing layer as possible. The wound was closed and a transfusion given. Later I regretted very bitterly that I had not made more sure of hæmostasis by either ligaturing the carotid in the neck or clipping it right across intracranially.

Although at first blush, it seems to be a dangerous step to clip or ligature the carotid intracranially there is in truth extremely little difference between that and tying it in the neck. The ophthalmic artery is the only important branch given off between these two sites of election if we disregard the very small branches to the pars glandularis of the pituitary. However, that the possible anastomotic channel is of some importance is shown by the fact that in three fistulous aneurysms in which I have tied the artery in the neck and in the head as well, the vision in the ipsilateral eye has not been lost, which speaks well for the collaterals of the ophthalmic artery. The most disturbing feature of intracranial carotid ligature is that if the patient were to become hemiparetic it is next to impossible to take the clip off again.

The course of the case under discussion was that she did excellently and was transferred to the Convalescent Branch 9.10.39 but six days later she suddenly bled again, this time into the ventricles and died on the twenty-ninth day after operation. The neck of the aneurysm had given way again. The specimen was lost when the Surgical Research Department was destroyed by enemy action shortly afterwards. In the afterthought it is clear that nothing would have saved the patient but two clips on the carotid intracranially, one above and one below the origin of the aneurysm. It is not known, of course, whether she would have survived that procedure.

CASE II.—Miss M. P., aged 29. The writer was asked to see this patient in 1932 by his colleague Dr. Hilliard Holmes. She was then aged 14 and a few days before she had had a severe subarachnoid hæmorrhage proved by lumbar puncture, after which a third nerve palsy had appeared. The question of ligature was discussed but was not proceeded with because we were, as we would now think, unnecessarily pessimistic about its risks. It was thought that even if nothing was done, her chances of survival were, at the worst, very fair. This proved to be a correct conjecture. For the first five years she did housework and for the next seven she worked as a nurse. Her oculomotor palsy had never quite recovered and at times she used to have severe pain in the forehead and inner canthus lasting for days on end. On 29.9.46 she had a "faint" and fell, losing consciousness for half an hour. She had very severe pains in her head and neck and was readmitted to the Manchester Royal Infirmary under Professor Oliver as a probable fresh rupture of her aneurysm. The C.S.F. was, however, clear, cells 7, protein 30. Skull X-rays showed a small shell of calcification slightly above and to the right of the posterior clinoid process. This was evidently the old aneurysm of nearly fifteen years ago. Angiography 19.10.46 by my Chief Assistant, Mr. A. N. Guthkelch, showed that it was not thrombosed since thorotrast entered the sac. He accordingly tied the common carotid artery and four weeks later the internal. No untoward signs followed and she was discharged, more free from pain than she had been for many years.

These two cases demonstrate how an aneurysm may in young persons persist for years before it causes urgent symptoms again and that although in the meantime the wall has calcified in part the cavity has not been obliterated by thrombosis. In neither of these patients did the original third nerve palsy fully recover in the intervals of twelve and fourteen and a half years respectively between their hospital admissions.

LIST OF THIRD NERVE ISOLATED ANEURYSMAL PALSIES, 55 CASES.

Year	Initials	Sex	Age	Subarach. hæm.	Angiogram	Ligature	Present state
1927	P. N.	M	42	+	—	Exploration	Died, few days
"	A. S.	F	21	+	+	Pack (1939)	" 1939 (Case I)
1932	F. I.	F	46	+	—	—	Well in 1940
"	M. P.	F	14	+	+	I.C.A. (1946)	Alive 1947 (Case II)
1933	L. C.	F	57	+	+	C.C.A.	" 1947
1935	A. S.	F	37	+	+	I.C.A.	" "
"	M. S.	F	56	—	+	C.C.A.	" "
1936	A. E.	F	54	+	—	C.C.A.	Died in hosp.
"	M. C.	M	52	—	—	—	" heart 1938
"	H. V.	M	45	+	—	C.C.A.	" 1943
1937	J. B.	F	42	+	—	C.C.A.	" few days
"	J. C.	M	37	+	+	I.C.A.	Alive 1947
"	M. F.	F	64	—	+	C.C.A.	Well four years later

Year	Initials	Sex	Age	Subarach. hæm.	Angiogram	Ligature	Present state
1937	L. J.	F	40	+	−	−	Untraced
,,	N. S.	F	32	+	−	−	,,
,,	W. P.	M	60	−	−	−	Died 1944
1938	J. H.	F	51	+	−	−	Untraced
,,	D. C.	F	33	+	−	C.C.A.	Alive 1947
,,	E. B.	M	67	−	−	−	Died 1942
,,	M. B.	F	17	+	+	−	,, 1 month later
,,	M. E.	F	62	+	−	−	,, 1 year later
1939	A. B.	M	36	+	+	−	Well 1947
,,	D. C.	M	43	+	−	−	Died in hosp.
,,	E. F.	F	56	+	−	C.C.A.	,, ,,
,,	M. K.	M	40	+	−	Pack + C.C.A.	Alive and well
,,	J. T.	M	35	+	−	Clip	Died in hosp.
,,	E. W.	F	74	−	−	−	Untraced
1940	N. C.	F	51	+	−	−	Well 1947
,,	R. R.	F	40	−	−	−	Died in hosp.
,,	S. S.	F	76	−	+	−	Well 1942
1941	E. M.	F	48	−	−	−	,, 1947
,,	A. S.	F	51	+	+	Pack	,, ,,
,,	S. T.	F	57	+	−	−	
1942	T. G.	F	60	−	+	C.C.A.	Well 1947
1943	D. C.	F	46	+	−	−	,, ,,
,,	D. P.	M	56	−	−	−	,, ,,
,,	G. R.	M	41	+	+	I.C.A.	,, ,,
,,	A. G.	F	45	+	+	C.C.A.	,, ,,
,,	A. T.	F	62	−	−	−	Alive 1947
1944	A. C.	F	51	+	+	I.C.A.	Well 1947
,,	R. C.	F	45	−	+	−	,, ,,
,,	M. F.	F	61	+	−	−	,, ,,
,,	M. K.	F	60	−	−	−	,, ,,
,,	J. N. S.	M	13	+	−	I.C.A.	,, ,,
,,	H. W.	M	52	+	+	C.C.A.	,, ,,
1945	E. E.	F	40	+	+	C.C.A.	,, ,,
,,	A. G.	F	46	+	−	−	Unknown
,,	E. H.	F	50	+	−	−	Well 1947
,,	K. T.	M	26	+	+	I.C.A.	,, ,,
1946	R. C.	M	46	+	+	Abandoned	Hemiparesis Well 1947
,,	A. T.	M	46	+	+	−	Well 1947
,,	A. T.	M	31	−	−	−	,, ,,
,,	N. S.	F	64	+	+	C.C.A.	,, ,,
,,	N. T.	F	56	+	+	C.C.A.	,, ,,
,,	J. M.	M	47	+	+	I.C.A.	,, ,,

C.C.A. = Common carotid artery (15 ligations). I.C.A. = Internal carotid artery (8 ligations).

ARTERIOSCLEROTIC ANEURYSMS

Besides the congenital aneurysms there is another group, larger than is often realized, in older people with arteriosclerosis; its size is only impressive in a large series of cases (cp. Berger, 1923; Saphir, 1933). Five of my isolated third nerve palsies were hypertensives and in the whole series were 15 such patients, about 10%. The prognosis is naturally graver, but old though they often are, they do not die as quickly or universally as might be imagined, as the appended table shows.

Moderate hypertension is not an absolute contra-indication to ligature, though the majority must be refused. The internal carotid of one and the common of another have been tied with survival—for eight years in the first, the second has been done only six months. This is a much lower proportion of ligatures than in the more usual type with normal ranges of blood-pressure. The supposed increased speed of the intracranial circulation in hypertension might be taken as favourable to the establishment of a collateral circulation but against this must be set the state of the arteries themselves, for in many the lumen is so much reduced by endarterial proliferation that any supposed benefit conferred by speed is in fact more than offset by diminution of flow. Angiography may help in making visible the calibre of the vessels, but some are obviously such poor risks that the clinician can make up his mind without angiography that the aneurysm is incurable and must be left to its fate. Even then some of the patients die not from rupture of their aneurysm but from angina or myocardial failure. This has happened in 4 of my own cases.

15 PATIENTS WITH ANEURYSM, HYPERPIESIS AND ARTERIOSCLEROSIS.

1937	B. Mrs.	57	220/150	Subclinoid aneurysm (Lig. I.C.A.)	Died 1946. Heart
„	P. Mr.	60	190/120	(Third n. palsy)	„ 1944. Angina
„	W. Mr.	57	195/140	(Sixth + trigem.)	Alive
1938	B. Mr.	67	250/150	(Third n.)	Died 1942. Heart
„	H. Mrs.	—	190/115	(Third and sixth n.)	Untraced
1939	W. Mrs.	74	220/130	Subclinoid	„
1940	B. Mrs.	66	200/110	Subclinoid	Alive
„	H. Mrs.	63	220/100	(Third n.)	„
„	S. Mrs.	76	180/110	(Third n.)	Untraced after 1941
1941	B. Mr.	66	250/130	—	Died 1943. Pneumonia
„	H. Mrs.	67	250/120	(Sixth + trigem.)	Alive
1943	C. Mrs.	67	210/130	Fistulous subarach.	Died 1944
„	T. Mrs.	62	200/115	(Third and sixth n.)	Alive
1944	F. Mrs.	61	230/110	(3 hæms.)	„
1946	S. Mrs.	56	200/120	(Third n.) Lig. C.C.A.	„

In Cases 1 and 15 the carotid was successfully tied.

DIFFERENTIAL DIAGNOSIS

It must be reiterated that this paper concerns itself with paralysis of the oculomotor nerve alone without coincident lesions of others of the cranial nerves. This removes from consideration a number of possible ætiological agents. At different times in the past all manner of causes have been suggested for third nerve palsy: cold, debility, rheumatism of the sphenoidal (superior orbital) fissure, sinusitis, syphilis, neuritis, diabetes, disseminated sclerosis, brain tumour, almost anything except aneurysm. A man can only speak authoritatively from his own experience and the writer's has been that there has been only one really frequent cause, namely aneurysm, and this he has taught for many years. It was the strength of this conviction which led to the first known exploration for aneurysm in 1927. At this date the relationship was recognized by few others. Of other causes, there is a group due to head injury, either directly or from expanding clot and a very few caused by brain tumours. Isolated third nerve palsy is not often seen with brain tumours and when it occurs the mechanism is usually herniation of the temporal lobe into the tentorial hiatus (Jefferson, 1937). In 3 cases a frank palsy with complete ptosis resulted from a pituitary tumour but it was never then unassociated with chiasmal and other neurological signs. Only twice has a positive Wassermann reaction been present, and that without an aneurysm, for the reaction was negative in the whole 158 cases of the aneurysmal series. Of course, taking the diplopias by and large, disseminated sclerosis and myasthenia gravis would account for the majority but these diseases do not cause pure, unilateral and complete third nerve palsies. It is the completeness of the paralysis in the vast majority that is so characteristic of aneurysm. The aneurysm, because of the relationship of carotid and oculomotor nerve, always seems to press on the nerve severely enough to interrupt entirely its conduction for a time, at all events. It cannot be said that the exceptions are never met with, recovery occasionally manifests itself quickly and by the time the case is seen the palsy may be partial. But the patients almost invariably say that the behaviour of the eye has been such that a total palsy at one time could safely be inferred.

Another important feature is that the onset of paralysis is speedy, a matter of hours or, at the most, days and that it is always accompanied by very severe pain in the distribution of the first trigeminal division, and especially at the inner canthus. The only disorder which exactly mimics aneurysmal paralysis of the third nerve is periodic or intermittent third nerve palsy. I will not attach the term "ophthalmoplegic migraine" to this condition for I feel that knowledge is not advanced by including one condition which I do not fully understand in another almost equally obscure. Edwin Bramwell (1934) did much to extract the aneurysms from these vague clinical groupings. It is true that periodic oculomotor palsy is a condition that, like migraine, begins in youth and is associated with headache but its cause is purely conjectural. I have seen half a dozen or so cases, one of whom had had 30 attacks of oculomotor palsy. Angiograms have been made on 4 with absolutely negative results. The vessels were of excellent calibre, their distribution was normal and there was no sign of angiospasm. The difference between these cases and aneurysmal compression is that in the periodic palsies the nerve usually recovers so completely that an entirely fresh palsy is possible and may be repeated time after time. In the aneurysms the recovery after a single episode is never complete enough for so strikingly fresh a palsy to present itself. It is in this disparity between the degrees of recovery that the key to differentiation usually lies.

Even if after many attacks some permanent defect in oculomotor function persists there will still be the history of earlier attacks with complete return of function. Nor is that all, for although aneurysms can occur in youth and even in babyhood as I have briefly illustrated it is rarely that they do so, whereas the periodic palsies usually start in childhood. Further still, not only the completeness but the rapidity of the recovery gives a further differentiating clue.

A condition which also may mimic aneurysm, though the similitude is nearer with infra- than with supra-clinoid aneurysms, is carcinoma or endothelioma of the nasopharynges. The symptomatology of neurological complications caused by invasion of the skull base has recently been described by Erik Godtfredsen (1944) in an admirable monograph. Curiously, Godtfredsen does not consider aneurysm in his differential diagnosis, though the mimicry can be nearly but not absolutely exact. I have found difficulty in not more than 3 cases because there is usually a striking difference in the initial and in the dominant signs of the two conditions which can be systematized thus:

A. Isolated oculomotor palsy never occurs with nasopharyngeal carcinoma as the only sign.

B. In nasopharyngeal tumours the commonest nerve involved is the trigeminal (71%, Godtfredsen) and of the motor nerves to the eyeball the abducens is the one most often paralysed. This is quite different from the cavernous aneurysm syndrome where lesions of trigeminus are associated with palsy not only of the sixth nerve but of the third and fourth as well.

C. With nasopharyngeal tumours paralysis of the ninth to twelfth cranial nerves not uncommonly accompanies ocular palsies. This could only happen with basilar or vertebral aneurysms; third nerve palsies are rare in the first and absent in the second of these sources.

D. Metastatic deposits in the cervical glands, often unilateral, are very common in nasopharyngeal tumours; they never, of course, occur with aneurysms.

In angiography we have a method of differential diagnosis which is very reliable but it should be added that plain X-rays will sometimes show calcification in the aneurysmal wall, though not until it has been there for some years. In one patient whose carotid I tied in 1935 no calcification was then present, but in 1945 on review the aneurysmal wall could be clearly seen reproducing to a nicety the angiographic appearances of ten years before. In another case (Case II) reviewed twelve years after the aneurysm first made its appearance the wall was also calcified but in this case the vessel had not been ligatured. The importance of this case is that it shows the calcification is not in itself a sign that the aneurysm is "dead", and further, since the patient was a girl of 16 when first seen, that calcification can occur in youth as well as in age. It should be added that erosion of the petrous bone may sometimes be seen in basal projection X-rays of patients suspected of malignant invasion. X-rays can thus assist in the diagnosis of either condition.

ANGIOGRAPHY

A brief comment will suffice for a subject on which there are already several monographs and important papers (Moniz, 1927, 1931, 1933; Reichert, 1943; Engeset, 1944; List *et al.*, 1945). The first three angiograms that showed up aneurysms were all made independently in 1933 by Dott, Moniz and Lima, and the writer. Angiography is the surest way in which the presence of an aneurysm can be diagnosed and its exact site and dimensions made visible. It has been done in 24 cases. In fig. 4 A–E the silhouettes of a few cases are shown. It will be observed that the aneurysms look very similar, that they arise in much the same place, that most of them are situated posterior to the carotid trunk in the direction of the blood flow, taking into account the syphon bend of the carotid which Moniz was the first to demonstrate *in vivo*. In one case there is an anterior as well as a posterior aneurysm. This is rare. Irregularities in shape and in shadow density are due, not to peculiarities of external contour but to laminated clot inside. In other words, the angiogram is a picture of the inside of the aneurysm. In fig. 4 F no aneurysm was present but the horizontal part of the artery in the cavernous sinus is seen to be elevated above the skull floor. This was a case of nasopharyngeal tumour and the arteriogram demonstrates not only the absence of an aneurysm but an abnormality in the course of the carotid which is evidently running over a mound of tumour infiltrating the skull base. This was proved to be so at operation.

TREATMENT

This revolves round the question of carotid-ligature, a subject which has a huge literature of its own. The first surgeon to tie the carotid was Astley Cooper; his cases were aneurysms in the neck. The operation was first done for a carotico-cavernous aneurysm inside the skull by Benjamin Travers (1809). Krayenbühl (1941) says that the first operators for saccular aneurysms were Coe and Le Fort but in reality both these aneurysms were fistulous. Horsley (Beadles, 1907) seems to have been, in fact, the pioneer. Nor could an operation for saccular aneurysm have been performed before Horsley's day, until, that is, neurology was sufficiently advanced to differentiate the condition and neurosurgery sufficiently perfected to allow of verification during the life of the sufferer, relatively recent events.

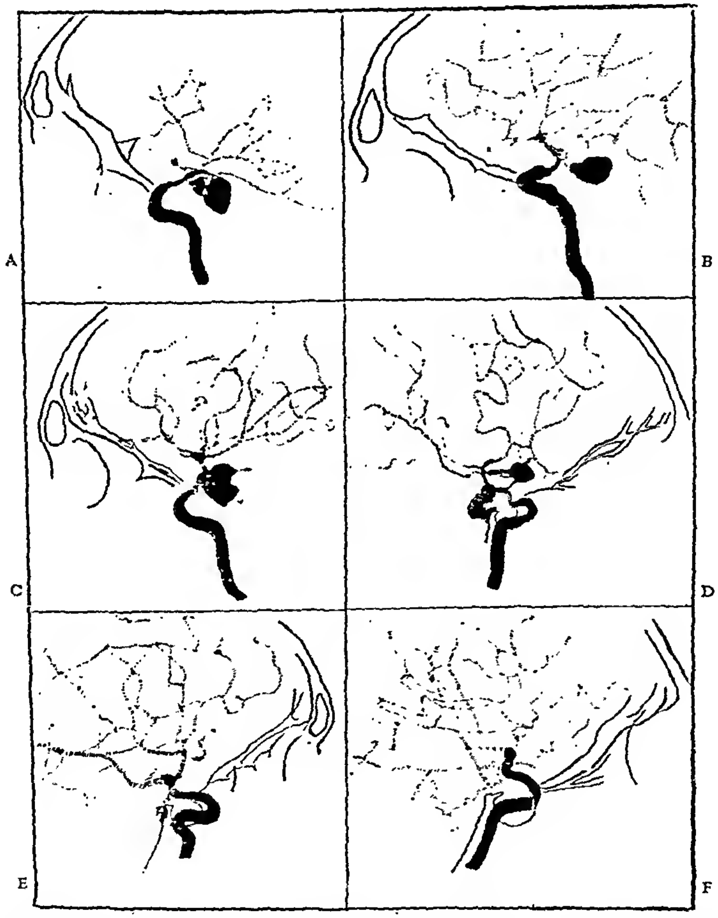


FIG. 4.—Angiograms of supraclinoid aneurysms (A–E). Elevation of carotid by invading nasopharyngeal tumour (F).

I will first deal with the alternatives to ligature. There are but two: (*a*) the packing of hammered muscle tissue transplant around the aneurysm (Dott, 1933; Jefferson, 1938); (*b*) the occlusion of the neck of the aneurysm by a silver clip at the point where it springs from the carotid (Dandy, 1944). I have used muscle packs three times, two patients survive, respectively five and four years, but in one I tied the common carotid two months after the pack, because he continued with pain, always a sign that the aneurysm is not securely thrombosed. In the *third* case (Case I, *see* p. 424) I had to pack muscle around the artery because the silver clip that I applied to the neck of the sac cut through, leading to a torrential hæmorrhage. This patient did well for a month and then died in a few hours from a recurrent hæmorrhage that broke through into the ventricles. This experience deflected me from further attempts to clip the neck of the sac and indeed, although it has many attractions, it is not a sound procedure because the wall close to the artery is, in the nature of things, friable and likely to give way when a metal band is applied. Dandy had the same experience and although he was the inventor of the method, and a courageous one it was, he seems to have become less enthusiastic and latterly preferred to put clips on the carotid above and below the point where the aneurysm left it.

This is a better method, for the main artery takes the clip well, but if a good collateral circulation is to be ensured, it requires that it should occlude the vessel below the posterior communicating artery, a matter of luck because that vessel can be seen.

In another case I applied a clip to the aneurysm but the patient died of operative wound infection. What other clips I have applied have been to occlude the carotid trunk intracranially in cases with carotico-cavernous fistulæ, the vessel being secured in the neck as well.

The operations alternative to the clipping of the neck of the sac are (*a*) ligature of the artery in the neck, (*b*) ligature or occlusive clipping of the carotid trunk inside the skull. There is little to choose between them. In all of the cases operated on, other than those mentioned above, the carotid trunk usually the common, sometimes the internal, has been tied in the neck. In a few we have used the two-stage method of tying the common first and the internal after an interval. The common carotid seems to have done as well as the internal carotid ligatures, probably because the subarachnoid aneurysms are usually small and thrombose readily if the circulation is slowed for a time.

This operation has been done in 23 cases of the present series by myself or my associates—G. F. Rowbotham, James Hardman, J. Schorstein, R. A. Bailey, D. Farley and A. N. Guthkelch. Of these patients all survive but one who died seven years later from an unknown cause and 3 who died very quickly from intracerebral bleeding (*see* Schorstein, 1940). An attempt to tie the carotid was made in 3 other cases but had to be abandoned because hemiplegic signs appeared within five to fifteen minutes of closing the vessel. There are some who say that this never happens if the Matas' test of percutaneous compression is negative. This is not true. It is difficult to see why it should occur unless the tightening of the ligature on the vessel sets up a spasm of the vessel intracranially. It might prove to be the case that if the ligature were left on the hemiplegic signs would disappear but it would be a risky experiment. Possibly periarterial sympathectomy and carotid body strip (Olivercrona, 1944) are worth while but I have not tried them yet.

Three of the cases died, as I have said, within a day or so of ligature. They were all emergency ties in semi-comatose patients and were experimental. These examples were described by Schorstein in his 1940 paper. Despite adverse criticism by Dandy, I still believe that the work that Schorstein (1940) did in my Department on carotid ligature is correct. He concluded that cerebral anoxia rather than thrombosis is the chief danger and that thrombosis or embolism have been incorrectly believed to be the prime factors. When it is remembered that in about 8% of individuals the circle of Willis is wanting in some part, the failure of some patients to "take" a ligature is not surprising. The most serious anomaly is the origin of both anterior cerebrals from one side, and that the side to be ligatured.

In all, we have ligatured one or other carotid fifty times and the three deaths mentioned were the only fatalities. Of the 23 ties for supraclinoid aneurysms, the 19 survivors are all well, though the recovery of the oculomotor nerve has never been absolute. The oldest survivor is now 71, having had her carotid tied in 1933. The youngest was a boy of 12 who two years ago had had a hæmorrhage after his oculomotor palsy developed and was in hospital when a fresh hæmorrhage started. The internal carotid was ligatured with success. We had the mortification of seeing one patient die in hospital from intraventricular rupture whilst awaiting operation. I am convinced that patients rarely die from subarachnoid hæmorrhage alone, not at least quickly. I am sure that Richardson and Hyland (1941) are right when they say that in the majority of apparently plain subarachnoid bleedings there is some hæmorrhage into the adjacent brain. Its mass or its situation may quickly cause death and is the most usual reason for it.

An important word must be added about the cases on whom no operation was performed Why were some left alone? There were two main causes, first that some were aged hypertensives with arteriosclerotic vessels, secondly because patients refused operation when they were told the risks. No patient who had severe pain refused but there were several who had long got over the worst and were only referred to hospital because of residual ptosis or diplopia. On the whole it must be confessed that these patients have done well. It is an important conclusion that patients can survive by natural processes. Upon what grounds, then, can a patient be left to his own defences? I have come to regard pain as the most dangerous sign in aneurysms and would make the decision considerably on that factor; so far few patients who remained pain-free came to any harm whether operated upon or not. But the decision to do nothing would be much fortified if an arteriogram showed conclusively that the sac was small or difficult to see clearly as is the case when it is well filled with clot. This has happened twice and the carotids were not tied. The patients gave characteristic histories but were pain free. They remain well.

CONCLUSIONS

(1) The commonest cause of isolated oculomotor palsy is supraclinoid carotid aneurysm.

(2) In the writer's personal series of 158 intracranial aneurysms, the conjunction was seen in 55.

(3) Valuable information as to shape, size, position and origin can be obtained by angiography and by no other method.

(4) Persistent pain is the most informative sign of activity in the aneurysm.

(5) Carotid ligature is not only a satisfactory but a reasonably safe procedure. Of 19 patients who survived ligature only one has since died, seven years later. The others are alive thirteen, twelve and less years after operation.

(6) The characteristics of oculomotor palsies as exhibited by these cases are discussed.

REFERENCES

ALBRIGHT, J. (1929) *Johns Hopk. Hosp. Bull.*, 44, 215.
BEADLES, C. F. (1907) *Brain*, 30, 285.
BERGER, L. (1923) *Virchow's Arch.*, 245, 138.
BRAMWELL, E. (1934) *Trans. ophthal. Soc. U.K.*, 54, 205.
BRINTON, D. (1852) *Trans. path. Soc. Lond.*, 3, 49.
CONWAY, J. (1926) *Brit. J. Ophthal.*, 10, 78.
DANDY, W. (1944) Intracranial Arterial Aneurysms. Baltimore.
DOTT, N. (1932–33) *Trans. med.-chir. Soc. Edinb.*, 47, 219.
ENGESET, A. (1944) Cerebral Angiography with Perabrodil. Oslo.
EPPINGER, H. (1887) *Arch. klin. Chir.*, 35 (suppl.).
FEARNSIDES, E. G. (1916) *Brain*, 39, 224.
FORBUS, W. (1930) *Johns Hopk. Hosp. Rep.*, 47, 239.
FRANCE, J. F. (1846) *Guy's Hosp. Rep.*, 4, 46.
GARVEY, P. H. (1934) *Arch. Ophthal., N.Y.*, 9, 1032.
GODTFREDSEN, E. (1944) Ophthalmologic and Neurologic Symptoms in Malignant Nasopharyngeal Tumours. Copenhagen.
GULL, W. (1859) *Guy's Hosp. Rep.*, 5, 281.
JEFFERSON, G. (1937) *Brain*, 60, 444.
—— (1938) *Brit. J. Surg.*, 26, 267.
KRAYENBÜHL, H. (1941) Das Hirnaneurysmata, Zürich.
LIST, C. F., BURGE, C. H., and HODGES, F. S. (1945) *Radiology*, 45, 1.
MAHONEY, W., and SHEEHAN, D. (1936) *Arch. Neurol. Psychiat., Chicago*, 35, 99.
McDONALD, C. A., and KORB, M. (1939) *Arch. Neurol. Psychiat., Chicago*, 42, 298.
MILETTI, M. (1946) *Riv. oto-neuro-oftalm.*, 21, 1.
MONIZ, E. (1927) *Rev. neurol.*, 34 (ii), 72.
—— (1931) Diagnostic des tumeurs cérébrale et épreuve de l'encéphalographie artérielle, Paris.
—— (1933) *Rev. Oto-Neuro-Ophtal.*, 11, 745.
NATTRASS, F. S. (1928) *Edinb. med. J.*, 35, 30.
OLIVECRONA, H. (1944) *Acta chir. scand.*, 91, 353.
PEACOCK, T. B. (1876) *St. Thom. Hosp. Rep.*, 119, 317.
REICHERT, TR. (1943) Die Arteriographie der Hirngefässe. Berlin.
RICHARDSON, J. C., and HYLAND, H. H. (1941) *Medicine, Baltimore*, 20, 1.

ROGERS, L. (1946) *R. J. nav. med. Serv.*, 32, 270.
SAPHIR, M. (1933) *Amer. J. Ophthal.*, 16, 110.
SCHORSTEIN, J. (1940) *Brit. J. Surg.*, 28, 50.
SZEKELY, J. (1928) *Beitr. Gesch. Med.*, 8, 162.
SYMONDS, C. P. (1923) *Guy's Hosp. Rep.*, 73, 139.
—— (1924) *Quart. J. Med.*, 18, 93.
TRAVERS, B. (1810) *Med.-chir. Trans.*, 2, 1.
VON HOFFMAN (1894) *Wien. klin. Wschr.*, 7, 823.

Cases were shown and discussed but owing to shortage of space the following are recorded here by title only:

(1) Right and Left Iridocyclitis, ? Sympathetic. (2) Retinitis Pigmentosa with Bitemporal Hemianopia. (3) Infantile Glaucoma in a Child of 3 Months—Bilateral Iridectomy. (4) Congenital Coloboma of the Iris and Choroid, with Cataracts, Left Intracapsular Extraction.—Shown by Mr. R. STEWART SCOTT (for Mr. T. MILNES BRIDE).

Boeck's Sarcoid.—Dr. W. STIRLING.

(1) Phakomatosis. (2) Ptosis with Pseudo-Graefe Phenomenon. (3) Krukenberg's Spindle. (4) Pseudoglioma.—Dr. G. RENWICK.

(1) Pigmentation of Conjunctiva. (2) Iris Inclusion—Intracapsular Extraction of Lens. (3) Undifferentiated Malignant Neoplasm of Inner Canthal Region. (4) Fulminating Exophthalmic Ophthalmoplegia.—Dr. O. M. DUTHIE.

Atypical Pigmentary Degeneration of the Retina.—Dr. S. B. SMITH.

(1) Neuroretinitis of Undetermined Ætiology. (2) Gross Esophoria, Corrected Surgically.—Dr. F. JANUS.

Section of Urology

President—R. H. O. B. Robinson, F.R.C.S.

[*January* 23, 1947]

The following cases and specimens were shown:

Squamous Metaplasia in Papillary Carcinoma of the Kidney.—Mr. E. W. Riches.

Kidney Showing Calculi and Tuberculosis.—Professor R. J. Willan.

Hypoplastic Kidney and Hyperpiesia.—Mr. A. Wilfrid Adams.

(1) Retroperitoneal Fibrosarcoma Completely Enveloping the Kidney. (2) Unusual Ruptured Kidney.—Mr. Howard G. Hanley.

An "Early" Renal Cancer Showing Calcification.—Mr. Hugh Donovan.

Anaplastic Hypernephroma with Calculus and Hydronephrosis.—Mr. J. D. Fergusson.

Hydatid Disease of the Kidney (Two Cases).—Mr. Clifford Morson.

(1) Hydatids of the Kidney. (2) Hydatids of the Bladder. (3) Hydatids Passed in Micturition.—Mr. F. R. Kilpatrick.

Uretero-colic Anastomosis.—Mr. Hugh Donovan.

A Hazard of Uretero-intestinal Anastomosis.—Mr. Howard G. Hanley.

Carcinoma of the Ureter.—Mr. J. D. Fergusson.

Achalasia of the Uretero-vesical Orifice and Pyelitis of Pregnancy.—Mr. J. H. Carver.

Diverticulum of the Bladder (Two Cases: One Male, One Female).—Mr. Harold Dodd.

(1) Hairpin in Male Bladder. (2) X-ray of Pencil in Female Bladder. (3) X-ray of Paper Clip in Wall of Male Bladder.—Mr. A. W. Badenoch.

Leiomyoma of Bladder treated by Cystectomy.—Mr. Henry Vernon.

Preputial Fistula.—Mr. A. Wilfrid Adams.

[*February* 27, 1947]

DISCUSSION ON THE USE OF PENICILLIN IN UROLOGY

Dr. A. L. P. Peeney, *Department of Clinical Pathology and Bacteriology, Birmingham United Hospital:* The assessment of the value of penicillin in urology may be carried out under two headings, namely as a prophylactic agent, or for the treatment of active infections.

The position of penicillin in prophylaxis can best be determined by a long-term statistical survey and it is intended to undertake such an investigation in the near future. The purpose of this paper, however, is to consider only the possibilities of penicillin in the treatment of those patients in whom active infection is established, excluding cases of venereal disease.

The important points governing penicillin treatment are the degree of sensitivity of the infecting organism to penicillin, and whether the indicated concentration of the drug can be maintained in that system of the body in which the infection occurs.

In the genito-urinary field many infections are due to Gram-negative bacilli or *Streptococcus fæcalis*, but comparatively few detailed studies have been made of these common invaders of the urinary tract. The early literature (Fleming, 1929; McKee and Rake, 1942; Hobby, Meyer and Chaffee, 1942) contains many references to the insensitivity to penicillin of these bacterial species, with little attempt to determine if there is any variation in their degree of resistance.

Bornstein (1940) examined 27 strains of *Streptococcus fæcalis* and found them all insensitive to a concentration of 8 units of penicillin per c.c., whereas Helmholz and Sung (1944) by a viable count technique, demonstrated the bactericidal effect of 3 units of penicillin per c.c. for *Streptococcus fæcalis* and of 8 units of penicillin per c.c. for Proteus. Coliform organisms they found of intermediate sensitivity between these bacterial species and the highly resistant forms such as *Bact. aerogenes* and *Ps. pyocyanea.*

The technique of determination of sensitivity to penicillin is important. The usual methods, such as ditch plate, cup plate or filter paper discs do not offer very close correlation with fluid titrations which, as a rule, show bacteriostasis with much smaller concentrations of penicillin than do the common solid media methods. For this reason the sensitivity tests recorded in this paper were carried out in fluid titrations in 1 c.c. quantities and the minimum bacteriostatic concentration was the lowest concentration of penicillin which prevented visible growth of a small inoculum when incubated overnight. No attempt was made to demonstrate penicillinase production since Bondi and Dietz (1944) have shown that the inability to produce penicillinase is not a factor in determining sensitivity to penicillin, though they pointed out that organisms forming the enzyme were not likely to be highly susceptible.

It was decided to limit the upper range of the titration to 200 units of penicillin per c.c., as this was considered the maximum concentration which could be reasonably maintained in the urine with moderate economy of penicillin. Tables I and II show the penicillin dilution ranges used in the titrations, and the minimum bacteriostatic concentration for 215 strains isolated from urinary cultures. Approximately 53% of Gram-negative bacillary forms are sensitive to concentrations of penicillin which can be maintained in the urine, but all strains of *Ps. pyocyanea* examined were resistant. On the other hand, Gram-positive cocci, including *Streptococcus fæcalis*, were much more sensitive to penicillin, with fewer resistant strains.

TABLE I.—MINIMUM BACTERIOSTATIC CONCENTRATION (UNITS OF PENICILLIN PER C.C.) OF 138 STRAINS OF GRAM-NEGATIVE BACILLI ISOLATED FROM URINES.

	Units of penicillin per c.c.												
Strain	>200	200	166	133	100	83	66	50	33	16	8	<8	Total
Coliform organisms	32	4	6	10	7	10	4	3	3	1	1	—	81
Paracolon bacilli	—	—	—	1	—	—	1	—	—	—	—	—	2
Proteus morgani	16	1	—	—	—	—	—	1	3	2	1	—	24
Proteus vulgaris	4	—	—	2	1	—	2	1	2	—	5	1	18
Ps. pyocyanea	13	—	—	—	—	—	—	—	—	—	—	—	13
	65												138

TABLE II.—MINIMUM BACTERIOSTATIC CONCENTRATION (UNITS OF PENICILLIN PER C.C.) OF 77 STRAINS OF GRAM-POSITIVE COCCI ISOLATED FROM URINES.

	Units of penicillin per c.c.									
Strain	>200	12·5	10·0	7·5	5·0	2·5	1·0	0·5	<0·5	Total
Streptococcus fæcalis	—	—	1	5	12	4	—	—	—	22
Group D streptococci	—	—	—	2	1	1	—	—	—	4
Non-hæmolytic streptococci	—	—	—	1	—	—	—	—	4	5
Streptococcus viridans	—	—	—	—	—	—	—	—	8	8
Staphylococcus pyogenes	2	1	1	—	—	—	—	—	29	33
M. tetragenus	1	—	—	—	1	—	—	1	1	4
Sarcinæ	—	—	—	—	—	—	—	—	1	1
	3									77

Having established the degrees of sensitivity to penicillin of the common invaders, we must now consider what urine concentrations may be obtained with reasonable doses of penicillin. Florey and his co-workers (1941) first showed that parenteral injection of penicillin caused a high blood concentration followed by a sharp fall due to excretion in concentrated form in the urine. The excretion varies greatly in different individuals, possibly from 50% to 90%, and has been shown by Rammelkamp and Bradley (1943) with diodrast, and Beyer *et al.* (1944) with para-amino hippuric acid by tubule blockade methods, to be mainly tubular in type. The urine concentrations in a small group of cases following different doses of penicillin by intramuscular injection are shown in Table III. When the patient was receiving interrupted injections the specimen was collected at as long a period of time after the injection as possible. The urine was immediately filtered through a Seitz filter and the estimation carried out by a modification of Rammelkamp's (1942) technique.

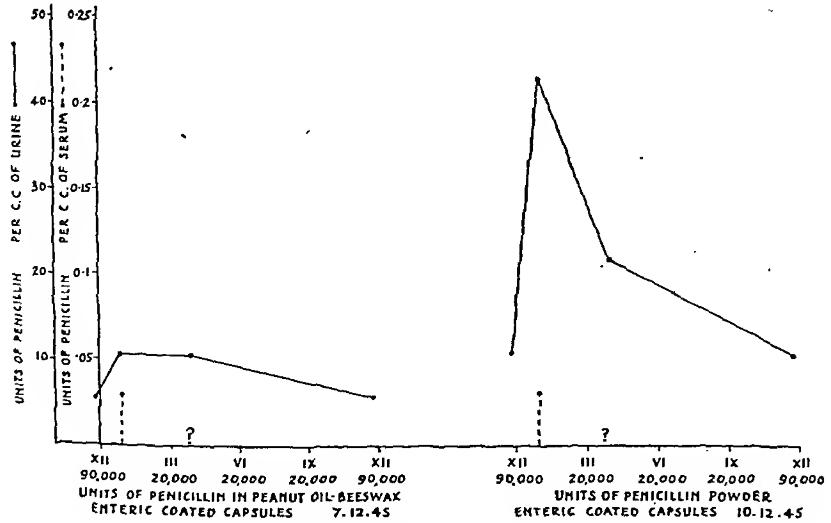
TABLE III.—URINE PENICILLIN CONCENTRATIONS AFTER ADMINISTRATION OF DIFFERENT DOSES.

Patient	Dose Units	Route of administration	Urine concentration Units per c.c.
M. K. ..	5,000	I.M. 3-hourly	12
H. K. ..	15,000	I.M. 3-hourly	21
S. K. ..	20,000	I.M. 3-hourly	42
S. K. ..	25,000	I.M. 3-hourly	83
J. G. ..	25,000	I.M. 3-hourly	64
H. F. ..	35,000	I.M. 3-hourly	83
J. N. ..	50,000	I.M. 3-hourly	85*
S. K. ..	200,000	I.M. C.D.	85
J. W. ..	400,000	I.M. C.D.	256

*Urine massively infected.

C.D.=Continuous drip, total fluid volume=100 c.c. in twenty-four hours.

The effect of oral administration by enteric coated capsules was also investigated in one case. The capsules used were of hard gelatin and received two coatings with liquor salol ether (B.P.C. 1911) which were allowed to dry between each application. Diagram I shows the blood and urine concentrations obtained when the capsules contained solid penicillin in peanut oil-beeswax mixture, as compared with similar capsules containing only penicillin powder without a slow release medium or antacid. The capsules were, as far as possible, administered to an empty stomach, and fluid intake restricted to 3 pints in twenty-four hours. Whenever feasible this regime of restricted controlled fluid intake was maintained for all the patients in this investigation.



ROMAN NUMERALS = time in hours. ? = less than lower limit of titration (0·03 unit per c.c.)

DIAGRAM I.

The single experiment suggests that once the acid reaction of the stomach has been negotiated it is advisable to have a preparation which is readily absorbed. It may be contended infecting organism to penicillin, and whether the indicated concentration of the drug can be maintained in that system of the body in which the infection occurs.

In the genito-urinary field many infections are due to Gram-negative bacilli or *Streptococcus fæcalis*, but comparatively few detailed studies have been made of these common invaders of the urinary tract. The early literature (Fleming, 1929; McKee and Rake, 1942; Hobby, Meyer and Chaffee, 1942) contains many references to the insensitivity to penicillin of these bacterial species, with little attempt to determine if there is any variation in their degree of resistance.

Bornstein (1940) examined 27 strains of *Streptococcus fæcalis* and found them all insensitive to a concentration of 8 units of penicillin per c.c., whereas Helmholz and Sung (1944) by a viable count technique, demonstrated the bactericidal effect of 3 units of penicillin per c.c. for *Streptococcus fæcalis* and of 8 units of penicillin per c.c. for Proteus. Coliform organisms they found of intermediate sensitivity between these bacterial species and the highly resistant forms such as *Bact. aerogenes* and *Ps. pyocyanea.*

The technique of determination of sensitivity to penicillin is important. The usual methods, such as ditch plate, cup plate or filter paper discs do not offer very close correlation with fluid titrations which, as a rule, show bacteriostasis with much smaller concentrations of penicillin than do the common solid media methods. For this reason the sensitivity tests recorded in this paper were carried out in fluid titrations in 1 c.c. quantities and the minimum bacteriostatic concentration was the lowest concentration of penicillin which prevented visible growth of a small inoculum when incubated overnight. No attempt was made to demonstrate penicillinase production since Bondi and Dietz (1944) have shown that the inability to produce penicillinase is not a factor in determining sensitivity to penicillin, though they pointed out that organisms forming the enzyme were not likely to be highly susceptible.

It was decided to limit the upper range of the titration to 200 units of penicillin per c.c., as this was considered the maximum concentration which could be reasonably maintained in the urine with moderate economy of penicillin. Tables I and II show the penicillin dilution ranges used in the titrations, and the minimum bacteriostatic concentration for 215 strains isolated from urinary cultures. Approximately 53% of Gram-negative bacillary forms are sensitive to concentrations of penicillin which can be maintained in the urine, but all strains of *Ps. pyocyanea* examined were resistant. On the other hand, Gram-positive cocci, including *Streptococcus fæcalis*, were much more sensitive to penicillin, with fewer resistant strains.

TABLE I.—MINIMUM BACTERIOSTATIC CONCENTRATION (UNITS OF PENICILLIN PER C.C.) OF 138 STRAINS OF GRAM-NEGATIVE BACILLI ISOLATED FROM URINES.

	Units of penicillin per c.c.												
Strain	>200	200	166	133	100	83	66	50	33	16	8	<8	Total
Coliform organisms	32	4	6	10	7	10	4	3	3	1	1	—	81
Paracolon bacilli	—	—	—	1	—	—	1	—	—	—	—	—	2
Proteus morgani	16	1	—	—	—	—	—	1	3	2	1	—	24
Proteus vulgaris	4	—	—	2	1	—	2	1	2	—	5	1	18
Ps. pyocyanea	13	—	—	—	—	—	—	—	—	—	—	—	13
	65												138

TABLE II.—MINIMUM BACTERIOSTATIC CONCENTRATION (UNITS OF PENICILLIN PER C.C.) OF 77 STRAINS OF GRAM-POSITIVE COCCI ISOLATED FROM URINES.

	Units of penicillin per c.c.									
Strain	>200	12·5	10·0	7·5	5·0	2·5	1·0	0·5	<0·5	Total
Streptococcus fæcalis	—	—	1	5	12	4	—	—	—	22
Group D streptococci	—	—	—	2	1	1	—	—	—	4
Non-hæmolytic streptococci	—	—	—	1	—	—	—	—	4	5
Streptococcus viridans	—	—	—	—	—	—	—	—	8	8
Staphylococcus pyogenes	2	1	1	—	—	—	—	—	29	33
M. tetragenus	1	—	—	—	1	—	—	1	1	4
Sarcinæ	—	—	—	—	—	—	—	—	1	1
	3									77

Having established the degrees of sensitivity to penicillin of the common invaders, we must now consider what urine concentrations may be obtained with reasonable doses of penicillin. Florey and his co-workers (1941) first showed that parenteral injection of penicillin caused a high blood concentration followed by a sharp fall due to excretion in concentrated

(1945) method. In view of the previous history of staphylococcal infections it was decided to use the dose scheme recommended by Bigger (1944) in the hope that we might eliminate both the urinary infection and any existing focus of staphylococci. She was accordingly given a continuous intramuscular drip of 400,000 units of penicillin in twenty-four hours by Eudrip apparatus, and fluid intake restricted to 3 pints during this period. A blood concentration of 0·75 unit per c.c. and a urine level of 256 units per c.c. were obtained. Within forty-eight hours of starting penicillin there was a marked reduction in the quantity of pus in the urine, bacteria were not seen in films of the centrifuged deposit, and cultures, after the addition of penicillinase prepared by Duthie's (1944) method, remained sterile. The treatment was maintained for five days and daily examination showed a progressive reduction in the pus cell content and consistently sterile cultures.

During the past two years there has been no recurrence either of the skin lesions or the pyelitis.

Comment.—The criticism may be offered that penicillin played no direct part in the cure of this patient, since cases of acute pyelitis with satisfactory drainage may be self-limiting. An unequivocal answer can only be provided by the investigation of a large series of cases.

CASE II.—M. R., female, aged 56. Was admitted to hospital 20.11.45 with a history of cystitis for the past twelve to fourteen years. This had been associated with considerable lower abdominal pain, intermittent hæmaturia, frequency and scalding on micturition. Cystoscopic examination by Mr. Donovan confirmed the presence of a very severe cystitis just as the late Sir John Thompson-Walker apparently had found ten years earlier in this case. The urine contained many pus cells and Gram-negative bacilli, and cultures yielded a growth of *Proteus morgani*, which was sensitive to 50 units of penicillin per c.c.

She was treated by the instillation into the bladder twice daily of 100 c.c. of saline containing 200 units of penicillin per c.c., and instructed to retain this for as long as possible. Five days after the treatment started a catheter specimen of urine showed no pus and a very scanty growth of Morgan's bacillus. Treatment was continued for fourteen days at which time there was no pyuria and cultures were sterile.

She was discharged from hospital 21.12.45 free from symptoms and with a clean urine. A letter from this patient twelve months later informed us that she felt extremely well and complained of no urinary symptoms whatsoever.

Comment.—This most unusual method of treatment was decided on because the patient was extremely averse to injections, and it is possible that the favourable result was somewhat fortuitous. The obvious contra-indication to this form of therapy is repeated catheterization with the attendant risk of the introduction of penicillin-insensitive micro-organisms.

Stul (1945) investigated 22 cases of Proteus infection of the urinary tract and considered the effect of usual urinary disinfectants, lavage and chemotherapy to be uncertain. This type of urinary infection is probably worthy of an extensive trial with penicillin by injection, though not necessarily by the instillation technique.

CASE III.—J. N., male, aged 29, a Dutch N.C.O., was admitted to the hospital following D-day with an automatic bladder due to a penetrating wound of spine in the upper thoracic region. There was considerable residual urine. Cultures showed a massive urinary infection containing large numbers of *Proteus vulgaris*, atypical Morgan's bacilli, diphtheroid organisms, *Staphylococcus aureus* (coagulase negative), non-hæmolytic streptococci, coliform organisms and *Streptococcus viridans*.

The Gram-positive organisms were all found to be sensitive to low concentrations of penicillin (less than 0·1 unit per c.c.), the proteus was sensitive to 8 units per c.c., the atypical Morgan's bacillus and the coliform were insensitive to concentrations of 200 units of penicillin per c.c. He was treated by penicillin, 50,000 units three-hourly intramuscularly, which produced a concentration of 85 units per c.c. At the end of five days the urine still contained pus and a large number of red blood cells; in smear a fairly large number of Gram-negative bacilli, and cultures yielded a heavy growth of coliform organisms, pyocyaneus, Morgan's bacillus and diphtheroids. These organisms were tested for sulphathiazole sensitivity and it was found that the coliforms were sensitive to 5 mg.%, the diphtheroids to 50 mg.% and the *Ps. pyocyanea* insensitive to the latter concentration. He was, therefore, treated with heavy doses of sulphathiazole and although the urine thirteen days after showed large numbers of Gram-negative bacilli, the only organism recovered in culture was *Ps. pyocyanea*, which is generally insensitive to penicillin and sulphonamide. Chemotherapy was discontinued and within the space of a few weeks the urine was once again heavily infected with mixed bacterial types.

Comment.—Although it was felt that the patient's condition would render permanent sterilization of the urinary tract impossible, the case report is included because it shows the close correlation which may be obtained between *in vitro* findings and *in vivo* results.

CASE IV.—B. R., female, aged 39. Admitted to hospital 5.2.45 with a history of frequency of micturition for three years and incontinence of urine for three days prior to admission. Cystoscopic examination showed an extremely irritable bladder with leukoplakia. The urine contained a moderate number of pus cells and occasional red blood cells, with many Gram-negative bacilli and a small number of streptococci. Cultures yielded a heavy growth of *Proteus vulgaris* (sensitive to 66 units of penicillin per c.c.) and a moderate number of *Streptococcus viridans* (sensitive to 0·08 unit of penicillin per c.c.). The patient was given a continuous intramuscular drip by Eudrip of 200,000 units of that similar urine and blood values could have been obtained by other methods of oral administration, but we were not so greatly concerned to define the best technique for oral treatment as to confirm that levels effective for the *Streptococcus fæcalis* could be readily obtained in the urine by oral administration.

Many investigators have reported on the oral use of penicillin: Little and Lumb (1945) combined it with raw egg, Perlstein *et al.* (1945) with lanoline and corn oil in capsules, McDermott *et al.* (1945) in each of the following substances—corn oil, water, preceded by magnesium trisilicate and in peanut oil-beeswax. All the workers observed that the resultant blood and urine levels showed considerable wastage as compared with parenteral injection. Seager *et al.* (1946), investigating the effect of oral penicillin, used resin-coated capsules, and found that three to six times the intramuscular dose was necessary to produce equal blood concentrations. Nevertheless, since penicillin is now freely available, we agree with Heatley (1945) that the convenience of oral administration will, in some cases, more than compensate for the larger amounts of the drug required. This it would seem applies more especially to urinary infections by all except the most resistant bacterial species.

Before passing to a review of clinical cases, it might be of interest to examine the effect on the blood and urine of a single large injection of penicillin, at the same time emphasizing that groups of individuals exhibit quite marked variations in the rate of excretion of penicillin and consequently in their blood and urine levels when followed over a period of hours. Diagram II shows the effect of 100,000 units of penicillin in 2 c.c. of saline intramuscularly.

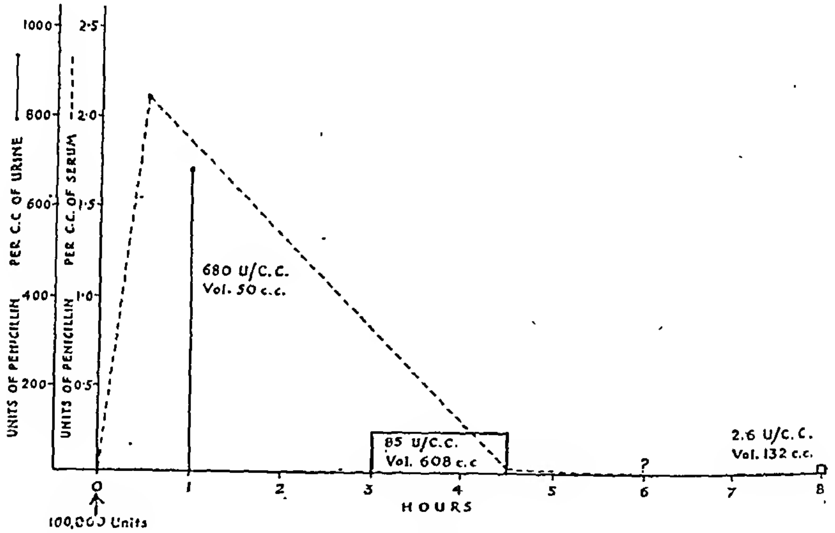


DIAGRAM II.—Urine and blood concentrations after intramuscular injection of 100,000 units of penicillin.

The bladder was emptied immediately before the injection. It will be seen that although there was a blood "peak" of 2·1 units of penicillin per c.c. at thirty minutes, there was only 0·03 unit per c.c. at four and a half hours, and at six hours the concentration was below the limits of titration (0·03 unit per c.c.). On the other hand, the urine collected one hour after the injection showed 680 units per c.c. (34% excretion), and a specimen collected at eight hours was still actively bacteriostatic for all fully sensitive bacteria. The total excretion over the eight-hour period was approximately 86%. It would appear that a dose of this order at six to eight-hourly intervals should yield in most cases a urinary concentration adequate for the majority of strains of *Streptococcus fæcalis*.

The following is a description of a selected small group of treated cases.

CASE I.—J. W., female, aged 34. Long history of frequent recurrent boils and abscesses from one of which a staphylococcus was isolated and found to be sensitive to 0·04 unit of penicillin per c.c. She was admitted urgently to hospital on 13.3.45 with a provisional diagnosis of perinephric abscess, where she was found to have fever, pain in the loin, frequency and slight dysuria. The urine showed a marked pyuria and heavy infection with *B. coli*, which was sensitive to a concentration of 83 units of penicillin per c.c., and insensitive to 5 mg. of sulphathiazole per 100 c.c. by Harper and Cawston's

(1945) method. In view of the previous history of staphylococcal infections it was decided to use the dose scheme recommended by Bigger (1944) in the hope that we might eliminate both the urinary infection and any existing focus of staphylococci. She was accordingly given a continuous intramuscular drip of 400,000 units of penicillin in twenty-four hours by Eudrip apparatus, and fluid intake restricted to 3 pints during this period. A blood concentration of 0·75 unit per c.c. and a urine level of 256 units per c.c. were obtained. Within forty-eight hours of starting penicillin there was a marked reduction in the quantity of pus in the urine, bacteria were not seen in films of the centrifuged deposit, and cultures, after the addition of penicillinase prepared by Duthie's (1944) method, remained sterile. The treatment was maintained for five days and daily examination showed a progressive reduction in the pus cell content and consistently sterile cultures.

During the past two years there has been no recurrence either of the skin lesions or the pyelitis.

Comment.—The criticism may be offered that penicillin played no direct part in the cure of this patient, since cases of acute pyelitis with satisfactory drainage may be self-limiting. An unequivocal answer can only be provided by the investigation of a large series of cases.

CASE II.—M. R., female, aged 56. Was admitted to hospital 20.11.45 with a history of cystitis for the past twelve to fourteen years. This had been associated with considerable lower abdominal pain, intermittent hæmaturia, frequency and scalding on micturition. Cystoscopic examination by Mr. Donovan confirmed the presence of a very severe cystitis just as the late Sir John Thompson-Walker apparently had found ten years earlier in this case. The urine contained many pus cells and Gram-negative bacilli, and cultures yielded a growth of *Proteus morgoni*, which was sensitive to 50 units of penicillin per c.c.

She was treated by the instillation into the bladder twice daily of 100 c.c. of saline containing 200 units of penicillin per c.c., and instructed to retain this for as long as possible. Five days after the treatment started a catheter specimen of urine showed no pus and a very scanty growth of Morgan's bacillus. Treatment was continued for fourteen days at which time there was no pyuria and cultures were sterile.

She was discharged from hospital 21.12.45 free from symptoms and with a clean urine. A letter from this patient twelve months later informed us that she felt extremely well and complained of no urinary symptoms whatsoever.

Comment.—This most unusual method of treatment was decided on because the patient was extremely averse to injections, and it is possible that the favourable result was somewhat fortuitous. The obvious contra-indication to this form of therapy is repeated catheterization with the attendant risk of the introduction of penicillin-insensitive micro-organisms.

Stul (1945) investigated 22 cases of Proteus infection of the urinary tract and considered the effect of usual urinary disinfectants, lavage and chemotherapy to be uncertain. This type of urinary infection is probably worthy of an extensive trial with penicillin by injection, though not necessarily by the instillation technique.

CASE III.—J. N., male, aged 29, a Dutch N.C.O., was admitted to the hospital following D-day with an automatic bladder due to a penetrating wound of spine in the upper thoracic region. There was considerable residual urine. Cultures showed a massive urinary infection containing large numbers of *Proteus vulgaris*, atypical Morgan's bacilli, diphtheroid organisms, *Staphylococcus aureus* (coagulase negative), non-hæmolytic streptococci, coliform organisms and *Streptococcus viridans*.

The Gram-positive organisms were all found to be sensitive to low concentrations of penicillin (less than 0·1 unit per c.c.), the proteus was sensitive to 8 units per c.c., the atypical Morgan's bacillus and the coliform were insensitive to concentrations of 200 units of penicillin per c.c. He was treated by penicillin, 50,000 units three-hourly intramuscularly, which produced a concentration of 85 units per c.c. At the end of five days the urine still contained pus and a large number of red blood cells; in smear a fairly large number of Gram-negative bacilli, and cultures yielded a heavy growth of coliform organisms, pyocyaneus, Morgan's bacillus and diphtheroids. These organisms were tested for sulphathiazole sensitivity and it was found that the coliforms were sensitive to 5 mg.%, the diphtheroids to 50 mg.% and the *Ps. pyocyonea* insensitive to the latter concentration. He was, therefore, treated with heavy doses of sulphathiazole and although the urine thirteen days after showed large numbers of Gram-negative bacilli, the only organism recovered in culture was *Ps. pyocyanea*, which is generally insensitive to penicillin and sulphonamide. Chemotherapy was discontinued and within the space of a few weeks the urine was once again heavily infected with mixed bacterial types.

Comment.—Although it was felt that the patient's condition would render permanent sterilization of the urinary tract impossible, the case report is included because it shows the close correlation which may be obtained between *in vitro* findings and *in vivo* results.

CASE IV.—B. R., female, aged 39. Admitted to hospital 5.2.45 with a history of frequency of micturition for three years and incontinence of urine for three days prior to admission. Cystoscopic examination showed an extremely irritable bladder with leukoplakia. The urine contained a moderate number of pus cells and occasional red blood cells, with many Gram-negative bacilli and a small number of streptococci. Cultures yielded a heavy growth of *Proteus vulgoris* (sensitive to 66 units of penicillin per c.c.) and a moderate number of *Streptococcus viridans* (sensitive to 0·08 unit of penicillin per c.c.). The patient was given a continuous intramuscular drip by Eudrip of 200,000 units of that similar urine and blood values could have been obtained by other methods of oral administration, but we were not so greatly concerned to define the best technique for oral treatment as to confirm that levels effective for the *Streptococcus fæcalis* could be readily obtained in the urine by oral administration.

Many investigators have reported on the oral use of penicillin: Little and Lumb (1945) combined it with raw egg, Perlstein *et al.* (1945) with lanoline and corn oil in capsules, McDermott *et al.* (1945) in each of the following substances—corn oil, water, preceded by magnesium trisilicate and in peanut oil-beeswax. All the workers observed that the resultant blood and urine levels showed considerable wastage as compared with parenteral injection. Seager *et al.* (1946), investigating the effect of oral penicillin, used resin-coated capsules, and found that three to six times the intramuscular dose was necessary to produce equal blood concentrations. Nevertheless, since penicillin is now freely available, we agree with Heatley (1945) that the convenience of oral administration will, in some cases, more than compensate for the larger amounts of the drug required. This it would seem applies more especially to urinary infections by all except the most resistant bacterial species.

Before passing to a review of clinical cases, it might be of interest to examine the effect on the blood and urine of a single large injection of penicillin, at the same time emphasizing that groups of individuals exhibit quite marked variations in the rate of excretion of penicillin and consequently in their blood and urine levels when followed over a period of hours. Diagram II shows the effect of 100,000 units of penicillin in 2 c.c. of saline intramuscularly.

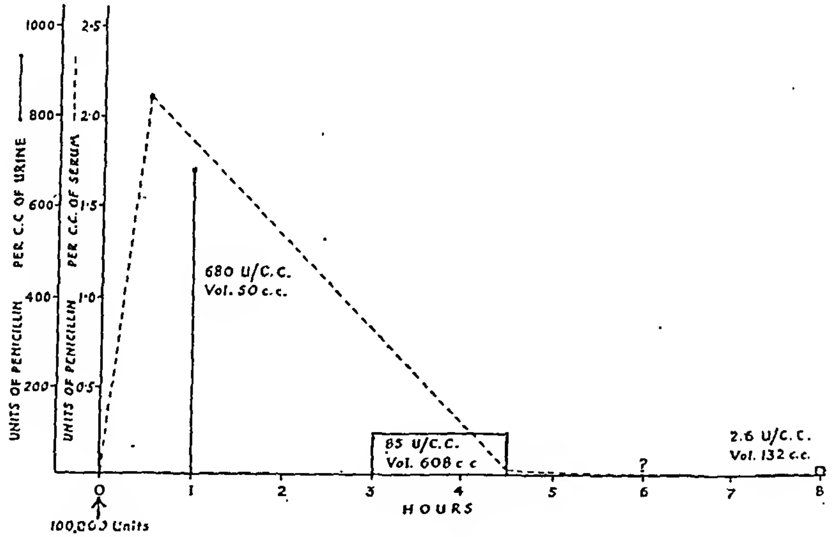


DIAGRAM II.—Urine and blood concentrations after intramuscular injection of 100,000 units of penicillin.

The bladder was emptied immediately before the injection. It will be seen that although there was a blood "peak" of 2·1 units of penicillin per c.c. at thirty minutes, there was only 0·03 unit per c.c. at four and a half hours, and at six hours the concentration was below the limits of titration (0·03 unit per c.c.). On the other hand, the urine collected one hour after the injection showed 680 units per c.c. (34% excretion), and a specimen collected at eight hours was still actively bacteriostatic for all fully sensitive bacteria. The total excretion over the eight-hour period was approximately 86%. It would appear that a dose of this order at six to eight-hourly intervals should yield in most cases a urinary concentration adequate for the majority of strains of *Streptococcus fæcalis.*

The following is a description of a selected small group of treated cases.

CASE I.—J. W., female, aged 34. Long history of frequent recurrent boils and abscesses from one of which a staphylococcus was isolated and found to be sensitive to 0·04 unit of penicillin per c.c. She was admitted urgently to hospital on 13.3.45 with a provisional diagnosis of perinephric abscess, where she was found to have fever, pain in the loin, frequency and slight dysuria. The urine showed a marked pyuria and heavy infection with *B. coli*, which was sensitive to a concentration of 83 units of penicillin per c.c., and insensitive to 5 mg. of sulphathiazole per 100 c.c. by Harper and Cawston's urinary symptoms. It would appear, therefore, that the *Streptococcus fæcalis* is a probable urinary pathogen.

That being so, this case is recorded as showing the effect which may be obtained by the use of penicillin, and in this patient the only operative therapy was by virtue of the urine concentration, since the blood levels were at all significant times below those necessary for inhibition of the *Streptococcus fæcalis*, as shown by *in vitro* tests.

It is noteworthy that *Streptococcus fæcalis* is usually resistant to all sulphonamide compounds so far available.

We have not had the opportunity to treat essentially intra- and peri-renal infections with penicillin, but since the majority of such infections are staphylococcal in nature, the results obtained should be directly conditioned by the sensitivity of the causal strain to the drug. Handfield-Jones (1946) states that in adults the results of penicillin treatment of perinephric abscess are dramatic, with rapid resolution and healing. In carbuncle the results are usually good, but treatment must be continued for at least three to four weeks if relapse is to be avoided. He stresses that pyelographic control is essential in addition to ordinary criteria of cure. Fort (1946) reports the cure of a case of perinephric cellulitis following an abscess of the index finger, by penicillin without suppuration or incision. Signs and symptoms and X-ray findings were clearly those of perinephric cellulitis.

It would appear from reports in the literature that abacterial pyuria does not respond to penicillin. Moore (1945) states that this condition resists all forms of therapy except organic arsenical preparations, and Bodner (1945) reported the case of a patient with this condition resistant to both sulphonamide and penicillin treatment who rapidly responded to mapharsan. Baines (1947) has had similar experiences.

It will be obvious from what has already been stated that we are only at the beginning of our investigations of the position of penicillin in genito-urinary infections, but it must be evident that such infections can only be treated adequately when the closest collaboration exists between the clinician and the bacteriologist. In all cases it is essential reliably to determine the sensitivity of the infecting organism to penicillin, to control by estimation that the necessary concentration is being maintained in the urine, and to assess the result of treatment, both clinically and bacteriologically. Even when such conditions obtain, it is almost certain that relapses will occur, due to anatomical deformity of the passages or the presence of inaccessible foci, possibly in calculi, deep crypts, prostatic abscesses or necrotic tissue, some of which would not be influenced even by high blood concentrations. We have treated a small number of patients with urinary calculi and infection, and although they have, on the whole, been materially improved, we have frequently failed completely to eradicate the urinary infection. This was almost certainly due in large measure to the calculus forming a reinfecting nidus.

Exley (1946) suggested that the presence of calculi in 8 cases investigated led to failure of penicillin to eliminate the infection, though 4 of these cases were cleared up with penicillin after the removal of the calculi. Bodner and Moulder (1945), however, were able to sterilize the urine of a patient with recurrent calculus formation and a staphylococcal infection with relatively small doses of penicillin after all other forms of therapy had failed. This patient's urine was still sterile and there was no evidence of recurrence of calculi nine months after discharge from hospital.

Nevertheless, in all urinary infections which resist other forms of treatment, and especially those due to the *Streptococcus fæcalis*, penicillin may afford the only satisfactory therapy. Similarly, penicillin should be considered in patients sensitive to the sulphonamides or where, for any other reason, the use of these drugs is precluded.

It may be that streptomycin with its wider range of activity against the Gram-negative bacillary forms may offer better possibilities, but it is not free from toxic effects and so far is in very short supply. I would prefer to look forward to the time when penicillin may be synthesized, in the hope that by some rearrangement of its molecule we shall be given a product of wider activity and with increased stability, so that patients may be spared repeated injections and an equal degree of susceptibility be introduced into the ranks of the Gram-negative bacilli as now exists in those of the Gram-positive cocci.

It is a pleasure to thank Professor A. P. Thomson, Dr. E. Bulmer, Mr. H. Donovan and Mr. Barnie-Adshead for permission to treat their patients and publish the case reports.

ADDENDUM.—Since this paper was read, a strain of *Streptococcus fæcalis* has been isolated from a urinary culture, which had a minimum bacteriostatic concentration of 33 units of penicillin per c.c.

penicillin in 100 c.c. of saline in twenty-four hours. The urine forty-eight hours later showed that the streptococcus had been eradicated but that the Proteus organism was still present in moderate numbers. The urine penicillin concentration was only 32 units per c.c. and the blood level 0·30 unit per c.c. As previously shown by *in vitro* test, the urine concentration was insufficient to inhibit the growth of the strain of Proteus present. The dose of penicillin was therefore raised to 400,000 units daily, and remained so for seven days—this increased the urine level to 64 units per c.c. Two days after increasing the dose, the urine was found to contain small amounts of pus, but no organisms were seen. Cultures, however, yielded a scanty growth of *Ps. pyocyanea* (insensitive to 1,000 units per c.c.) and *Bact. anaerogenes* (insensitive to 500 units per c.c.). Frequent subsequent urine examinations showed a progressive increase of the pyuria and Gram-negative bacillus content, and cultures repeatedly yielded a growth of the two resistant bacteria. The pyocyaneus was found to be sensitive to 5 mg.% of sulphathiazole but the anaerogenes was insensitive to 50 mg.% of sulphathiazole and sulphamethazine and 15 mg.% of sulphadiazine. This patient was discharged on 15.3.45, on sulphathiazole, having had nine days of intramuscular penicillin treatment.

In view of the intractable cystitis, the patient was readmitted 11.6.46, and the urine findings closely resembled those found before penicillin treatment had been instituted. At operation for ureteric transplantation (Mr. H. Donovan) the ureters were found to be normal and he successfully carried out a bilateral simultaneous transplantation of the ureters into the pelvic colon. The patient was discharged, very much improved, 30.7.46.

Comment.—Although this patient's original infecting organisms were eradicated, she was unfortunately left with a mixed pyocyaneus and anaerogenes infection which was insensitive to penicillin. The gross anatomical change in the bladder greatly militated against the therapeutic possibilities of any treatment. Subsequent history proved such to be the case. Mr. Donovan transplanted the ureters into the pelvic colon.

CASE V.—H. W., male, aged 56. History of intermittent pyelitis since 1931. Cystoscopic examination by B. J. Ward in 1941 showed pyelitis and cystitis, and there was a heavy infection with an indeterminate pigment-producing coagulase-negative staphylococcus. No calculus. Considerable improvement with sulphapyridine. Readmitted 18.4.45. The staphylococcus was sensitive to 0·03 unit of penicillin per c.c. and there was considerable pyuria. He was treated with penicillin, 20,000 units three-hourly intramuscularly, and the urine was sterile after five days' treatment. Frequent relapses occurred and the patient was again readmitted 1.12.45. At this time he was stated to have become sensitive to sulphonamides. The urine contained many pus cells and Gram-positive cocci, and cultures yielded a heavy growth of *Staphylococcus pyogenes* which were sensitive to 0·03 unit of penicillin per c.c. In view of the high susceptibility of this organism to penicillin, it was decided to try the effect of oral penicillin in enteric-coated capsules. The blood and urine concentrations obtained were those shown in Diagram I. Within forty-eight hours the patient was free from symptoms, and after five days' treatment the urine contained no pus or bacteria. Discharged on 14.1.46. His condition relapsed three weeks after leaving but five days' oral penicillin, as an outpatient, again rendered the urine normal and the patient free from symptoms. It was considered that a deep-seated focus must be present and he was advised to be readmitted for surgical investigation of the genito-urinary tract. This he refused.

Comment.—In this case the originally isolated staphylococcus differed in its coagulase reaction from the strain present in the later stages, which suggests that the original invader had been effectively removed by the systemic penicillin. Nevertheless, it did not reduce his tendency to relapse. Although his infection was readily amenable to penicillin, we should have given him a much longer course of treatment, since there was the possibility of a deep-seated, relatively inaccessible, focus, either in the kidney or prostate. As pointed out by Handfield-Jones (1946), long courses of penicillin are indicated in certain intra-renal infections. Florey *et al.* (1941) described the oral administration of penicillin to a child of 6 months which cured a staphylococcal infection of the urinary tract.

CASE VI.—A. S., female, aged 46. Admitted for Cæsarean section; a living child was delivered. Seven days after the operation the urine was found to be heavily infected and stained films showed large numbers of Gram-positive cocci and cultures yielded a heavy growth of *Streptococcus fæcalis*. She was treated with sulphathiazole, 1 gramme six-hourly, for four days, but the urine showed no change. The *Streptococcus fæcalis* isolated from the second specimen was found to be insensitive to 5 mg.% of sulphathiazole but sensitive to 2·5 units of penicillin per c.c. It was decided to treat the patient with penicillin, but since she was feeding her baby, fluid intake could not be restricted and she was allowed 7 pints of fluid in twenty-four hours. On 20,000 units of penicillin three-hourly, her blood was shown to contain 0·06 unit of penicillin thirty minutes after the injection, and less than 0·03 unit two hours fifty-five minutes after injection. The total urine voided over one complete three-hour period was 122 c.c., and contained 8·5 units of penicillin per c.c. After forty-eight hours the centrifuged deposit of the urine showed no pus cells or organisms, and cultures, with penicillinase, remained sterile. A further examination at the end of five days gave similar findings. Penicillin was then discontinued. The slight frequency and dysuria which existed in the early stages had, by this time, completely disappeared and the patient felt very well.

Comment.—It may be asked whether *Streptococcus fæcalis* is really pathogenic. The answer to this would appear to be that cases are frequently encountered in which there is pyuria and the only organism recovered is a *Streptococcus fæcalis*. Such cases are usually associated with low-grade urinary symptoms. It would appear, therefore, that the *Streptococcus fæcalis* is a probable urinary pathogen.

That being so, this case is recorded as showing the effect which may be obtained by the use of penicillin, and in this patient the only operative therapy was by virtue of the urine concentration, since the blood levels were at all significant times below those necessary for inhibition of the *Streptococcus fæcalis*, as shown by *in vitro* tests.

It is noteworthy that *Streptococcus fæcalis* is usually resistant to all sulphonamide compounds so far available.

We have not had the opportunity to treat essentially intra- and peri-renal infections with penicillin, but since the majority of such infections are staphylococcal in nature, the results obtained should be directly conditioned by the sensitivity of the causal strain to the drug. Handfield-Jones (1946) states that in adults the results of penicillin treatment of perinephric abscess are dramatic, with rapid resolution and healing. In carbuncle the results are usually good, but treatment must be continued for at least three to four weeks if relapse is to be avoided. He stresses that pyelographic control is essential in addition to ordinary criteria of cure. Fort (1946) reports the cure of a case of perinephric cellulitis following an abscess of the index finger, by penicillin without suppuration or incision. Signs and symptoms and X-ray findings were clearly those of perinephric cellulitis.

It would appear from reports in the literature that abacterial pyuria does not respond to penicillin. Moore (1945) states that this condition resists all forms of therapy except organic arsenical preparations, and Bodner (1945) reported the case of a patient with this condition resistant to both sulphonamide and penicillin treatment who rapidly responded to mapharsan. Baines (1947) has had similar experiences.

It will be obvious from what has already been stated that we are only at the beginning of our investigations of the position of penicillin in genito-urinary infections, but it must be evident that such infections can only be treated adequately when the closest collaboration exists between the clinician and the bacteriologist. In all cases it is essential reliably to determine the sensitivity of the infecting organism to penicillin, to control by estimation that the necessary concentration is being maintained in the urine, and to assess the result of treatment, both clinically and bacteriologically. Even when such conditions obtain, it is almost certain that relapses will occur, due to anatomical deformity of the passages or the presence of inaccessible foci, possibly in calculi, deep crypts, prostatic abscesses or necrotic tissue, some of which would not be influenced even by high blood concentrations. We have treated a small number of patients with urinary calculi and infection, and although they have, on the whole, been materially improved, we have frequently failed completely to eradicate the urinary infection. This was almost certainly due in large measure to the calculus forming a reinfecting nidus.

Exley (1946) suggested that the presence of calculi in 8 cases investigated led to failure of penicillin to eliminate the infection, though 4 of these cases were cleared up with penicillin after the removal of the calculi. Bodner and Moulder (1945), however, were able to sterilize the urine of a patient with recurrent calculus formation and a staphylococcal infection with relatively small doses of penicillin after all other forms of therapy had failed. This patient's urine was still sterile and there was no evidence of recurrence of calculi nine months after discharge from hospital.

Nevertheless, in all urinary infections which resist other forms of treatment, and especially those due to the *Streptococcus fæcalis*, penicillin may afford the only satisfactory therapy. Similarly, penicillin should be considered in patients sensitive to the sulphonamides or where, for any other reason, the use of these drugs is precluded.

It may be that streptomycin with its wider range of activity against the Gram-negative bacillary forms may offer better possibilities, but it is not free from toxic effects and so far is in very short supply. I would prefer to look forward to the time when penicillin may be synthesized, in the hope that by some rearrangement of its molecule we shall be given a product of wider activity and with increased stability, so that patients may be spared repeated injections and an equal degree of susceptibility be introduced into the ranks of the Gram-negative bacilli as now exists in those of the Gram-positive cocci.

It is a pleasure to thank Professor A. P. Thomson, Dr. E. Bulmer, Mr. H. Donovan and Mr. Barnie-Adshead for permission to treat their patients and publish the case reports.

ADDENDUM.—Since this paper was read, a strain of *Streptococcus fæcalis* has been isolated from a urinary culture, which had a minimum bacteriostatic concentration of 33 units of penicillin per c.c.

REFERENCES

Baines, G. H. (1947) *Brit. J. Urol.*, **19**, 16.

Beyer, K. H., Woodward, R., Peters, L., Verwey, W. F., and Mattis, P. A. (1944) *Science*, **100**, 107.

Bigger, J. W. (1944) *Lancet* (ii), 497.

Bodner, H. (1945) *Urol. cutan. Rev.*, 49, 598.

—— and Moulder, M. K. (1945) *J. Urol.*, 54, 123.

Bondi, A., and Dietz, C. C. (1944) *Proc. Soc. exper. Biol. Med.*, 56, 135.

Bornstein, S. (1940) *J. Bact.*, 39, 383.

Duthie, E. S. (1944) *Brit. J. exper. Path.*, 25, 96.

Exley, M. (1946) *J. Urol.*, 55, 436.

Fleming, A. (1929) *Brit. J. exper. Path.*, **10**, 226.

Florey, H. W., Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., and Jennings, M. A. (1941) *Lancet* (ii), 177.

Fort, C. A. (1946) *J. Urol.*, 56, 121.

Handfield-Jones, R. M. (1946) Penicillin. London, 238.

Harper, G. J., and Cawston, W. C. (1945) *J. Path. Bact.*, 57, 59.

Heatley, N. G. (1945) *Lancet* (i), 590.

Helmholz, H. F., and Sung, C. (1944) *Amer. J. Dis. Child.*, 68, 236.

Hobby, G. L., Meyer, K., and Chaffee, E. (1942) *Proc. Soc. exper. Biol. Med.*, 50, 277.

Little, C. J. H., and Lumb, G. (1945) *Lancet* (i), 203.

McDermott, W., Bunn, P. A., Benoit, M., DuBois, R., and Hayes, W. (1945) *Science*, **101**, 228.

McKee, C. M., and Rake, G. (1942) *J. Bact.*, 43, 645.

Moore, T. (1945) *Brit. J. Urol.*, 17, 131.

Perlstein, D., Kluener, R. G., and Liebmann, A. J. (1945) *Science*, **101**, 66.

Rammelkamp, C. H. (1942) *Proc. Soc. exper. Biol. Med.*, 56, 950.

—— and Bradley, S. F. (1943) *Proc. Soc. exper. Biol. Med.*, 53, 30.

Seager, L. D., Shoemaker, W. G., Mulholland, S., Miller, R., Wells, G. R., and Barnes, K. B. (1946) *J. Urol.*, 56, 594.

Stul, Th. (1945) *Helvetica Chirurgica Acta*, **12**, 638.

Lady Florey: The intermittent intramuscular injection of penicillin is of such inconvenience that a great many efforts have been made to find other means which would have equally good therapeutic effects. A type of administration is required which can be given to patients while they live at home and can be carried on for long enough periods to ensure that the infection has been eliminated. The methods most widely investigated have been those of single daily injections of penicillin in a vehicle delaying absorption—usually 4·8% beeswax in peanut oil and of oral administration.

For infections of the urinary tract it is important to compare the percentage of the dose excreted in the urine by the different methods. It has been found that after intramuscular injections of aqueous solutions 65% to 80% of the dose is excreted in the urine; after injections of penicillin in beeswax and peanut oil 33% and after oral administration only 8% to 23% of the dose is found in the urine. There is thus no question as to which is the most efficient method of administration.

There is a possibility, however, that injections even of aqueous solutions can be spaced widely enough to make treatment practicable at home and over sufficiently long periods of time.

Amongst a dozen healthy young men lying in bed recovering from battle wounds, the urinary excretion of penicillin following a single intramuscular injection of 100,000 units was measured.

The following approximate figures were obtained:

3 to 4 hours after injection	3,000 to 5,000 units per 100 c.c.
12 hours after injection	140 to 700 units per 100 c.c.
20 hours after injection	2 to 400 units per 100 c.c.
24 hours after injection	0 to 100 units per 100 c.c.

These concentrations can be compared with the upper limits of sensitivity of the organisms found in urinary tract infections:

Gonococci Hæmolytic streptococci	up to 18 units per 100 c.c.
Staphylococci *Strept. viridans*	up to 500 units per 100 c.c.
Non-hæmolytic streptococci *Strept. fæcalis*	up to 2,000 units per 100 c.c.
Gram-negative organisms	?

so it can be seen that a single injection of 100,000 units in aqueous solution per twenty-four hours should be sufficient to rid the urinary tract of the most sensitive organisms, twelve-hourly injections should do the same for the next group but the remainder should require more frequent injections or higher individual doses.

The question of whether infections caused by Proteus, *Bact. coli* or *Ps. pyocyanea* can be permanently cured by penicillin still remains a moot point. Use of local applications of penicillin in wounds in concentrations well above those found in the urine did not have any effect in reducing the percentage of cultures free of these organisms except in the case of coliform organisms, and here the amount was so slight as to be attributable to chance.

A very interesting outcome of this study of Gram-negative flora in wounds was the association between the appearance of *Staph. aureus* and the disappearance of all three species. A warning is issued in consequence that the treatment of a streptococcal or staphylococcal infection of the urinary tract by penicillin may end in a condition in which the main infecting organisms are Proteus, *Bact. coli* or *Ps. pyocyanea.*

These latter observations lead one to emphasize the close interrelation between mechanical and bacteriological factors in any infection. Obstruction caused by calculi or strictures, a foreign body, or slough, an atonic or fibrotic bladder or loculated pus will be responsible for the continuance of infection irrespective of the amount or duration of chemotherapy. The functions of surgery and chemotherapy are therefore closely linked in treatment, and responsibility for achieving a cure should rarely be placed entirely on one or the other.

Mr. Clifford Morson pointed out the importance of giving large doses of penicillin. He described the case of a woman of 61 who for fifteen years had suffered from one-hourly frequency of micturition due to a systolic bladder. Cystoscopy revealed a small ulcer above the right ureteric orifice and a bladder capacity of 2 oz. The organism isolated from the urine was the *Staph. aureus* which proved to be penicillin sensitive. As there was some doubt about the nature of the ulcer it was excised by open operation. Fortunately the pathologist reported that it was non-malignant. When the wound had nearly healed, a ten-day course of penicillin was given, the first dose being 150,000 units and the two subsequent doses 100,000 units, followed by 50,000 units at three-hourly intervals. The urine became sterile after forty-eight hours and the bladder capacity steadily increased so that now over two years since the treatment she can hold her urine for three hours. He gave an account of another case to illustrate the danger of the replacement of a penicillin-sensitive organism by one which was penicillin resistant. A dental surgeon was referred to him three years ago on account of bilateral hydronephrosis complicated by a *Staph. aureus* infection which caused so much urgency of micturition as to necessitate his retirement from practice. One injection of 50,000 units of penicillin followed at three-hourly intervals by 20,000 units for five days caused the disappearance of the *Staph. aureus*, but there followed an acute attack of *Bacillus coli* infection. The latter has been resistant to all kinds of drug treatment and his condition to-day is no better than it was three years ago.

Mr. Yates Bell agreed with Lady Florey that with insufficient penicillin dosage staphylococci were eliminated in early urine specimens without a decrease in the *B. coli*, which, however, decreased as the staphylococcus increased in later specimens.

His attention had been drawn to the long periods (six months or more) that an indwelling urethral catheter was tolerated in paraplegic cases without the development of a urethritis and therefore with a decrease in urinary infection; and for the past two years had accordingly used penicillin as a prophylactic in prostatic surgery during the period of indwelling catheter. During this time it had become possible to avoid two-stage operations (apart from rare

REFERENCES

Baines, G. H. (1947) *Brit. J. Urol.*, 19, 16.

Beyer, K. H., Woodward, R., Peters, L., Verwey, W. F., and Mattis, P. A. (1944) *Science*, 100, 107.

Bigger, J. W. (1944) *Lancet* (ii), 497.

Bodner, H. (1945) *Urol. cutan. Rev.*, 49, 598.

—— and Moulder, M. K. (1945) *J. Urol.*, 54, 123.

Bondi, A., and Dietz, C. C. (1944) *Proc. Soc. exper. Biol. Med.*, 56, 135.

Bornstein, S. (1940) *J. Bact.*, 39, 383.

Duthie, E. S. (1944) *Brit. J. exper. Path.*, 25, 96.

Exley, M. (1946) *J. Ural.*, 55, 436.

Fleming, A. (1929) *Brit. J. exper. Path.*, 10, 226.

Florey, H. W., Abraham, E. P., Chain, E., Fletcher, C. M., Gardner, A. D., Heatley, N. G., and Jennings, M. A. (1941) *Lancet* (ii), 177.

Fort, C. A. (1946) *J. Urol.*, 56, 121.

Handfield-Jones, R. M. (1946) Penicillin. London, 238.

Harper, G. J., and Cawston, W. C. (1945) *J. Path. Bact.*, 57, 59.

Heatley, N. G. (1945) *Lancet* (i), 590.

Helmholz, H. F., and Sung, C. (1944) *Amer. J. Dis. Child.*, 68, 236.

Hobby, G. L., Meyer, K., and Chaffee, E. (1942) *Proc. Soc. exper. Biol. Med.*, 50, 277.

Little, C. J. H., and Lumb, G. (1945) *Lancet* (i), 203.

McDermott, W., Bunn, P. A., Benoit, M., DuBois, R., and Hayes, W. (1945) *Science*, 101, 228.

McKee, C. M., and Rake, G. (1942) *J. Bact.*, 43, 645.

Moore, T. (1945) *Brit. J. Urol.*, 17, 131.

Perlstein, D., Kluener, R. G., and Liebmann, A. J. (1945) *Science*, 101, 66.

Rammelkamp, C. H. (1942) *Proc. Soc. exper. Biol. Med.*, 56, 950.

—— and Bradley, S. F. (1943) *Proc. Soc. exper. Biol. Med.*, 53, 30.

Seager, L. D., Shoemaker, W. G., Mulholland, S., Miller, R., Wells, G. R., and Barnes, K. B. (1946) *J. Urol.*, 56, 594.

Stul, Th. (1945) *Helvetica Chirurgica Acta*, 12, 638.

Lady Florey: The intermittent intramuscular injection of penicillin is of such inconvenience that a great many efforts have been made to find other means which would have equally good therapeutic effects. A type of administration is required which can be given to patients while they live at home and can be carried on for long enough periods to ensure that the infection has been eliminated. The methods most widely investigated have been those of single daily injections of penicillin in a vehicle delaying absorption—usually 4·8% beeswax in peanut oil and of oral administration.

For infections of the urinary tract it is important to compare the percentage of the dose excreted in the urine by the different methods. It has been found that after intramuscular injections of aqueous solutions 65% to 80% of the dose is excreted in the urine; after injections of penicillin in beeswax and peanut oil 33% and after oral administration only 8% to 23% of the dose is found in the urine. There is thus no question as to which is the most efficient method of administration.

There is a possibility, however, that injections even of aqueous solutions can be spaced widely enough to make treatment practicable at home and over sufficiently long periods of time.

Amongst a dozen healthy young men lying in bed recovering from battle wounds, the urinary excretion of penicillin following a single intramuscular injection of 100,000 units was measured.

The following approximate figures were obtained:

3 to 4 hours after injection	3,000 to 5,000 units per 100 c.c.
12 hours after injection	140 to 700 units per 100 c.c.
20 hours after injection	2 to 400 units per 100 c.c.
24 hours after injection	0 to 100 units per 100 c.c.

These concentrations can be compared with the upper limits of sensitivity of the organisms found in urinary tract infections:

Gonococci Hæmolytic streptococci	up to 18 units per 100 c.c.
Staphylococci *Strept. viridans*	up to 500 units per 100 c.c.
Non-hæmolytic streptococci *Strept. fæcalis*	up to 2,000 units per 100 c.c.
Gram-negative organisms	?

so it can be seen that a single injection of 100,000 units in aqueous solution per twenty-four hours should be sufficient to rid the urinary tract of the most sensitive organisms, twelve-hourly injections should do the same for the next group but the remainder should require more frequent injections or higher individual doses.

The question of whether infections caused by Proteus, *Bact. coli* or *Ps. pyocyanea* can be permanently cured by penicillin still remains a moot point. Use of local applications of penicillin in wounds in concentrations well above those found in the urine did not have any effect in reducing the percentage of cultures free of these organisms except in the case of coliform organisms, and here the amount was so slight as to be attributable to chance.

A very interesting outcome of this study of Gram-negative flora in wounds was the association between the appearance of *Staph. aureus* and the disappearance of all three species. A warning is issued in consequence that the treatment of a streptococcal or staphylococcal infection of the urinary tract by penicillin may end in a condition in which the main infecting organisms are Proteus, *Bact. coli* or *Ps. pyocyanea.*

These latter observations lead one to emphasize the close interrelation between mechanical and bacteriological factors in any infection. Obstruction caused by calculi or strictures, a foreign body, or slough, an atonic or fibrotic bladder or loculated pus will be responsible for the continuance of infection irrespective of the amount or duration of chemotherapy. The functions of surgery and chemotherapy are therefore closely linked in treatment, and responsibility for achieving a cure should rarely be placed entirely on one or the other.

Mr. Clifford Morson pointed out the importance of giving large doses of penicillin. He described the case of a woman of 61 who for fifteen years had suffered from one-hourly frequency of micturition due to a systolic bladder. Cystoscopy revealed a small ulcer above the right ureteric orifice and a bladder capacity of 2 oz. The organism isolated from the urine was the *Staph. aureus* which proved to be penicillin sensitive. As there was some doubt about the nature of the ulcer it was excised by open operation. Fortunately the pathologist reported that it was non-malignant. When the wound had nearly healed, a ten-day course of penicillin was given, the first dose being 150,000 units and the two subsequent doses 100,000 units, followed by 50,000 units at three-hourly intervals. The urine became sterile after forty-eight hours and the bladder capacity steadily increased so that now over two years since the treatment she can hold her urine for three hours. He gave an account of another case to illustrate the danger of the replacement of a penicillin-sensitive organism by one which was penicillin resistant. A dental surgeon was referred to him three years ago on account of bilateral hydronephrosis complicated by a *Staph. aureus* infection which caused so much urgency of micturition as to necessitate his retirement from practice. One injection of 50,000 units of penicillin followed at three-hourly intervals by 20,000 units for five days caused the disappearance of the *Staph. aureus*, but there followed an acute attack of *Bacillus coli* infection. The latter has been resistant to all kinds of drug treatment and his condition to-day is no better than it was three years ago.

Mr. Yates Bell agreed with Lady Florey that with insufficient penicillin dosage staphylococci were eliminated in early urine specimens without a decrease in the *B. coli*, which, however, decreased as the staphylococcus increased in later specimens.

His attention had been drawn to the long periods (six months or more) that an indwelling urethral catheter was tolerated in paraplegic cases without the development of a urethritis and therefore with a decrease in urinary infection; and for the past two years had accordingly used penicillin as a prophylactic in prostatic surgery during the period of indwelling catheter. During this time it had become possible to avoid two-stage operations (apart from rare mechanical failure to catheterize a patient), and the associated high mortality of suprapubic cystotomy. Penicillin was given as a routine, 100,000 units six-hourly, during pre-operative and post-operative periods of an indwelling catheter in association with chemotherapy if pyrexia developed. In view of Dr. Peeney's work increase of dosage to 200,000 units might be preferable, certainly if fever developed.

Mr. Edgar Freshman quoted a case of complete bladder paralysis following thrombosis of the veins of the spinal cord in which it seemed probable that the bladder would recover. The bladder was drained for seven weeks by an indwelling rubber catheter which was changed four times, and throughout the period of drainage he was given 100,000 units of penicillin and 1 gramme of sulphadiazine eight-hourly. His average fluid intake was over 100 oz. a day and he had no bladder irrigations. The urine was examined repeatedly, but remained sterile throughout the period of drainage, and there was no urethritis. His bladder gradually recovered its tone, and when he left hospital micturition was practically normal.

Mr. Hugh Donovan said that the use of penicillin to prevent infection after bladder surgery would need careful statistical study, which it was proposed to carry out. He had noted the practical abolition of post-operative chest complications when using penicillin as a routine urinary antiseptic. He could confirm that the bladder flora were penicillin resistant in a ward where penicillin had been much used. This was found to be the case in the Midland Regional Spinal Unit.

He pointed out that Helstrom had found masses of staphylococci in urinary calculi, even when the urine was sterile, and suggested that penicillin might improve the outcome of operation on bilateral staghorn stones.

Section of Physical Medicine

President—FRANK COOKSEY, O.B.E., M.D.

[*April* 9, 1947]

SAMUEL HYDE MEMORIAL LECTURE

Rheumatic Diseases: A Challenge And An Opportunity

By Professor HENRY COHEN, M.D., F.R.C.P.

> "Therefore the moon, the governess of floods,
> Pale in her anger washes all the air,
> That rheumatic diseases do abound."
> (Shakespeare: "Midsummer Night's Dream", Act II, Sc. 2.)

MY first duty is to express my deep and sincere gratitude for the honour your Council have done me by their invitation to deliver this lecture commemorating the work of the late Dr. Samuel Hyde of Buxton, who founded the British Balneological and Climatological Society, which is incorporated in this Section of Physical Medicine. Those who control the assigning of this notable and rare distinction, conferred on only six occasions in the past thirty-six years, have clearly been moved in to-day's choice, not by any inherent merit of mine but by the office of Chairman of the Ministry of Health's Advisory Subcommittee on Rheumatism which for the moment I happen to hold. I have therefore grasped this opportunity to examine afresh some of the major problems confronting those who seek to alleviate the sufferings of the victims of Medicine's neglected stepchild—the Rheumatic Diseases.

INCIDENCE

What is the size of the problem? The first serious effort in this country to find an answer to this question is embodied in a Report of the Ministry of Health published in 1924 of an investigation undertaken in 1922 [1]. This covered insured (N.H.I.) workers only. It was thus confined to manual workers and others earning less than £250 a year. As these categories embraced less than half the population (13½ million) and excluded housewives, the sample investigated was not fully representative. Moreover the rural districts, Wales, and the industrial North West (where rheumatic disease is thought to be prevalent) were poorly represented in this survey. Despite these limitations, which on the whole would tend to yield too small an incidence, the report reveals a problem of startling size. For this survey a number of practitioners were chosen and asked to record all patients consulting them for rheumatism. The total number of insured patients in the sample was 90,891; of these, in 1922, 42,288 (46·5%) consulted their doctors. A diagnosis of rheumatic disease was made in 2,510 (2·76% of the total). (This represents a "prevalence" and not an "attack" rate, i.e. a patient who had more than one attack during 1922 is counted only once in the incidence tables.) On the mechanical failure to catheterize a patient), and the associated high mortality of suprapubic cystotomy. Penicillin was given as a routine, 100,000 units six-hourly, during pre-operative and post-operative periods of an indwelling catheter in association with chemotherapy if pyrexia developed. In view of Dr. Peeney's work increase of dosage to 200,000 units might be preferable, certainly if fever developed.

Mr. Edgar Freshman quoted a case of complete bladder paralysis following thrombosis of the veins of the spinal cord in which it seemed probable that the bladder would recover. The bladder was drained for seven weeks by an indwelling rubber catheter which was changed four times, and throughout the period of drainage he was given 100,000 units of penicillin and 1 gramme of sulphadiazine eight-hourly. His average fluid intake was over 100 oz. a day and he had no bladder irrigations. The urine was examined repeatedly, but remained sterile throughout the period of drainage, and there was no urethritis. His bladder gradually recovered its tone, and when he left hospital micturition was practically normal.

Mr. Hugh Donovan said that the use of penicillin to prevent infection after bladder surgery would need careful statistical study, which it was proposed to carry out. He had noted the practical abolition of post-operative chest complications when using penicillin as a routine urinary antiseptic. He could confirm that the bladder flora were penicillin resistant in a ward where penicillin had been much used. This was found to be the case in the Midland Regional Spinal Unit.

He pointed out that Helstrom had found masses of staphylococci in urinary calculi, even when the urine was sterile, and suggested that penicillin might improve the outcome of operation on bilateral staghorn stones.

The most recent figures showing a heavy incidence are from Sweden where in 1923 Kahlmeter had reported that chronic articular rheumatism was the cause of retirement of 9% of insured workers. In 1944-45 Edström [4] investigated 72,000 persons—half in rural districts and half in villages—differing in social and economic status and environment. Of these 5,679 (7·9%) had rheumatic disease, and in 2,745 (3·8%) it was active; 480 (6·7 per 1,000) were permanently incapacitated.

It would be idle to claim that any of these statistical surveys is comparable with another or that from them can be gathered more than a general impression of the prevalence and morbidity of the rheumatic diseases. The samples examined are inadequate in number, type and variety; for example, the necessary omission of housewives from the 1924 English survey of insured persons is a cardinal defect. They refer to different age-groups, and different years in which the relative numbers in the different age-groups may vary. The differences in occupation, geography, climate and subsoil, social and economic status, nutrition and other significant features in these heterogeneous groups forbid strict comparison. There is a lack of differentiation of "attack" rate (morbidity incidence) and "prevalence" rate (morbidity prevalence). In some, e.g. the Social Surveys, the recorded diagnosis is usually that given by the subject of the interview; this self-diagnosis by those for whom any pain is "a touch of the rheumatics" is a flimsy basis for statistical records and analyses. It may indeed account for the fact previously noted, that in the most recent surveys half the population is recorded as suffering from non-incapacitating rheumatism. Finally, and of great importance, is the use in these reports of a varying nomenclature and classification of rheumatic disease, and the absence of any definitive criteria for the diagnosis of its diverse forms.

Any projected future surveys must take cognizance of all these points if they are to resist the attacks of the critics. In all fields of medicine the fallacies in interpreting the results of clinical investigations are a ready snare for the unwary. In rheumatic disease there is need for the greatest care not only in defining the results of observation but also in planning large-scale field and therapeutic experiments if they are to be most fruitful. To this end I would plead for the closest co-operation between the statistician and the clinician in this work. If this be achieved we shall hear less of the old gibe that "statistics may be made to tell anything, even the truth", and see fewer of those papers claiming, for a remedy in these diseases, 100% cures but written in that apologetic tone which is intended to convey that the author hopes to do better next time.

As an example of the tyranny of names and the absurd conclusions to which they may lead, let me quote, without acknowledgment for obvious reasons, a table from a recent paper, with the names of the collieries omitted.

Type of rheumatic ailment	Colliery A	B	C	Total
Rheumatoid arthritis..	8	5	9	22
Lumbago	5	10	13	28
Fibrositis	31	17	Nil	48
Sciatica	Nil	2	11	13
Neuritis	Nil	Nil	2	2

From an analysis of these figures which do not even specify the number of miners employed at each colliery so that an absolute and not a relative incidence alone can be seen, and without any diagnostic criteria for his differentiation of, for example, lumbago and fibrositis, the author concludes that as "there has not been observed a single case of fibrositis during the period of three months under review at Colliery C (the largest of the three)" this "surprising fact can be due to one thing only: Colliery C has pithead baths and the others have not". "This", he states, "is a striking illustration of the great medical value of such baths." But

evidence accumulated in this investigation it was concluded that the rheumatic diseases accounted for (1) nearly one-sixth of the total industrial invalidism in England and Wales; (2) an expenditure of £2,000,000 yearly in sickness benefit; and (3) a loss of 3,000,000 weeks of working time. Chronic arthritis was said to have been responsible for half the loss both in money and time.

An interesting community survey was made by Davidson and Duthie in 1937 in Aberdeenshire (2). It covered a population of 135,000. In an average winter month the total doctors' visits and consultations were 50,900 and of these 5,800 (11·4%) were for rheumatic disease. 875 were new cases; of these 672 were assigned to the muscular and neuritic groups, 68 to acute and subacute rheumatism, 82 to osteoarthritis and 53 to rheumatoid arthritis. The incidence in this series is higher than in many others; it may be explained by the adverse wintry climatic conditions of the north. But this work has one merit, rare in other surveys. In order to ensure, as far as practicable, uniformity of classification and diagnosis, Davidson and Duthie explained in detail to each practitioner taking part the criteria to be followed.

The Department of Health for Scotland in its Report on Chronic Rheumatic Diseases (1945) records significant morbidity statistics relevant to the year 1937-38 [2]. During this period, 1 in 50 insured men and 1 in 60 insured women were incapacitated by "muscular" rheumatism for a period of up to four weeks or by "neuritic" rheumatism for up to six weeks. The rheumatic diseases headed the incapacity tables with 3,000,000 days' incapacity, the digestive diseases (all forms) being second with 2,400,000 days. There were 45,300 new rheumatic cases of which 3,000 were articular in site and represented 270,000 days' incapacity but the ravages of arthritis are seen most strikingly in the fact that the disability of 1,600 patients incapacitated by arthritis in the preceding year continued throughout the period reviewed.

The most recent records for this country are to be found in the Social Health Surveys published in the Monthly Bulletin of the Ministry of Health and the Emergency Public Health Laboratory Service. These suggest that over 7% of the population is incapacitated by "rheumatism" for at least a day each year and that half the population suffers at some period of the year from "rheumatism" which is not disabling; but the figures, as recorded, are not wholly free from ambiguity. Figures from E.M.S. hospitals (1942-44) show that among Service patients about one-quarter of all rheumatic disease is arthritic at the age of 25, and that the proportion increases to one-third by the age of 45-50.

The incidence in other countries is revealing. In the National Health Survey of the United States in 1935-36, 6,850,000 (over 5%) of the population of 127,000,000 suffered from some form of rheumatic disease and of these 3,000,000 were arthritic [3]. Rheumatism was the commonest chronic illness of over a week's duration. It was twice as frequent as heart disease, seven times as frequent as cancer, and ten times as frequent as tuberculosis, but it ranked only fourteenth in the causes of death. Yet in 1935-36 it completely disabled 147,600 men and women in the United States (1·2 per 1,000 of the population) and another 800,000 were partially disabled to the extent of losing an average of five months' work each year. It is estimated that 100,000,000 days are lost yearly by partially and completely disabled victims, thus surpassing the loss arising from any other single cause. This figure for lost time due to rheumatism corresponds almost exactly, relative to the different populations of the two countries, with the 3,000,000 weeks of the 1924 report for England and Wales. At £4 a week in wages this represents a cost of £12,000,000 per annum to this country solely in work lost through disability; the total loss would be much greater if the costs of insurance benefits and medical care were included. A grave feature of the economic repercussions of rheumatism is that 50% of its victims are under 45 and should be at their optimum productive capacity; 70% are under 55—an age at which many workers are still at their most active.

The most recent figures showing a heavy incidence are from Sweden where in 1923 Kahlmeter had reported that chronic articular rheumatism was the cause of retirement of 9% of insured workers. In 1944-45 Edström [4] investigated 72,000 persons—half in rural districts and half in villages—differing in social and economic status and environment. Of these 5,679 (7·9%) had rheumatic disease, and in 2,745 (3·8%) it was active; 480 (6·7 per 1,000) were permanently incapacitated.

It would be idle to claim that any of these statistical surveys is comparable with another or that from them can be gathered more than a general impression of the prevalence and morbidity of the rheumatic diseases. The samples examined are inadequate in number, type and variety; for example, the necessary omission of housewives from the 1924 English survey of insured persons is a cardinal defect. They refer to different age-groups, and different years in which the relative numbers in the different age-groups may vary. The differences in occupation, geography, climate and subsoil, social and economic status, nutrition and other significant features in these heterogeneous groups forbid strict comparison. There is a lack of differentiation of "attack" rate (morbidity incidence) and "prevalence" rate (morbidity prevalence). In some, e.g. the Social Surveys, the recorded diagnosis is usually that given by the subject of the interview; this self-diagnosis by those for whom any pain is "a touch of the rheumatics" is a flimsy basis for statistical records and analyses. It may indeed account for the fact previously noted, that in the most recent surveys half the population is recorded as suffering from non-incapacitating rheumatism. Finally, and of great importance, is the use in these reports of a varying nomenclature and classification of rheumatic disease, and the absence of any definitive criteria for the diagnosis of its diverse forms.

Any projected future surveys must take cognizance of all these points if they are to resist the attacks of the critics. In all fields of medicine the fallacies in interpreting the results of clinical investigations are a ready snare for the unwary. In rheumatic disease there is need for the greatest care not only in defining the results of observation but also in planning large-scale field and therapeutic experiments if they are to be most fruitful. To this end I would plead for the closest co-operation between the statistician and the clinician in this work. If this be achieved we shall hear less of the old gibe that "statistics may be made to tell anything, even the truth", and see fewer of those papers claiming, for a remedy in these diseases, 100% cures but written in that apologetic tone which is intended to convey that the author hopes to do better next time.

As an example of the tyranny of names and the absurd conclusions to which they may lead, let me quote, without acknowledgment for obvious reasons, a table from a recent paper, with the names of the collieries omitted.

Type of rheumatic ailment	Colliery A	B	C	Total
Rheumatoid arthritis..	8	5	9	22
Lumbago	5	10	13	28
Fibrositis	31	17	Nil	48
Sciatica	Nil	2	11	13
Neuritis	Nil	Nil	2	2

From an analysis of these figures which do not even specify the number of miners employed at each colliery so that an absolute and not a relative incidence alone can be seen, and without any diagnostic criteria for his differentiation of, for example, lumbago and fibrositis, the author concludes that as "there has not been observed a single case of fibrositis during the period of three months under review at Colliery C (the largest of the three)" this "surprising fact can be due to one thing only: Colliery C has pithead baths and the others have not". "This", he states, "is a striking illustration of the great medical value of such baths." But

evidence accumulated in this investigation it was concluded that the rheumatic diseases accounted for (1) nearly one-sixth of the total industrial invalidism in England and Wales; (2) an expenditure of £2,000,000 yearly in sickness benefit; and (3) a loss of 3,000,000 weeks of working time. Chronic arthritis was said to have been responsible for half the loss both in money and time.

An interesting community survey was made by Davidson and Duthie in 1937 in Aberdeenshire (2). It covered a population of 135,000. In an average winter month the total doctors' visits and consultations were 50,900 and of these 5,800 (11·4%) were for rheumatic disease. 875 were new cases; of these 672 were assigned to the muscular and neuritic groups, 68 to acute and subacute rheumatism, 82 to osteoarthritis and 53 to rheumatoid arthritis. The incidence in this series is higher than in many others; it may be explained by the adverse wintry climatic conditions of the north. But this work has one merit, rare in other surveys. In order to ensure, as far as practicable, uniformity of classification and diagnosis, Davidson and Duthie explained in detail to each practitioner taking part the criteria to be followed.

The Department of Health for Scotland in its Report on Chronic Rheumatic Diseases (1945) records significant morbidity statistics relevant to the year 1937-38 [2]. During this period, 1 in 50 insured men and 1 in 60 insured women were incapacitated by "muscular" rheumatism for a period of up to four weeks or by "neuritic" rheumatism for up to six weeks. The rheumatic diseases headed the incapacity tables with 3,000,000 days' incapacity, the digestive diseases (all forms) being second with 2,400,000 days. There were 45,300 new rheumatic cases of which 3,000 were articular in site and represented 270,000 days' incapacity but the ravages of arthritis are seen most strikingly in the fact that the disability of 1,600 patients incapacitated by arthritis in the preceding year continued throughout the period reviewed.

The most recent records for this country are to be found in the Social Health Surveys published in the Monthly Bulletin of the Ministry of Health and the Emergency Public Health Laboratory Service. These suggest that over 7% of the population is incapacitated by "rheumatism" for at least a day each year and that half the population suffers at some period of the year from "rheumatism" which is not disabling; but the figures, as recorded, are not wholly free from ambiguity. Figures from E.M.S. hospitals (1942-44) show that among Service patients about one-quarter of all rheumatic disease is arthritic at the age of 25, and that the proportion increases to one-third by the age of 45-50.

The incidence in other countries is revealing. In the National Health Survey of the United States in 1935-36, 6,850,000 (over 5%) of the population of 127,000,000 suffered from some form of rheumatic disease and of these 3,000,000 were arthritic [3]. Rheumatism was the commonest chronic illness of over a week's duration. It was twice as frequent as heart disease, seven times as frequent as cancer, and ten times as frequent as tuberculosis, but it ranked only fourteenth in the causes of death. Yet in 1935-36 it completely disabled 147,600 men and women in the United States (1·2 per 1,000 of the population) and another 800,000 were partially disabled to the extent of losing an average of five months' work each year. It is estimated that 100,000,000 days are lost yearly by partially and completely disabled victims, thus surpassing the loss arising from any other single cause. This figure for lost time due to rheumatism corresponds almost exactly, relative to the different populations of the two countries, with the 3,000,000 weeks of the 1924 report for England and Wales. At £4 a week in wages this represents a cost of £12,000,000 per annum to this country solely in work lost through disability; the total loss would be much greater if the costs of insurance benefits and medical care were included. A grave feature of the economic repercussions of rheumatism is that 50% of its victims are under 45 and should be at their optimum productive capacity; 70% are under 55—an age at which many workers are still at their most active.

The most recent figures showing a heavy incidence are from Sweden where in 1923 Kahlmeter had reported that chronic articular rheumatism was the cause of retirement of 9% of insured workers. In 1944-45 Edström [4] investigated 72,000 persons—half in rural districts and half in villages—differing in social and economic status and environment. Of these 5,679 (7·9%) had rheumatic disease, and in 2,745 (3·8%) it was active; 480 (6·7 per 1,000) were permanently incapacitated.

It would be idle to claim that any of these statistical surveys is comparable with another or that from them can be gathered more than a general impression of the prevalence and morbidity of the rheumatic diseases. The samples examined are inadequate in number, type and variety; for example, the necessary omission of housewives from the 1924 English survey of insured persons is a cardinal defect. They refer to different age-groups, and different years in which the relative numbers in the different age-groups may vary. The differences in occupation, geography, climate and subsoil, social and economic status, nutrition and other significant features in these heterogeneous groups forbid strict comparison. There is a lack of differentiation of "attack" rate (morbidity incidence) and "prevalence" rate (morbidity prevalence). In some, e.g. the Social Surveys, the recorded diagnosis is usually that given by the subject of the interview; this self-diagnosis by those for whom any pain is "a touch of the rheumatics" is a flimsy basis for statistical records and analyses. It may indeed account for the fact previously noted, that in the most recent surveys half the population is recorded as suffering from non-incapacitating rheumatism. Finally, and of great importance, is the use in these reports of a varying nomenclature and classification of rheumatic disease, and the absence of any definitive criteria for the diagnosis of its diverse forms.

Any projected future surveys must take cognizance of all these points if they are to resist the attacks of the critics. In all fields of medicine the fallacies in interpreting the results of clinical investigations are a ready snare for the unwary. In rheumatic disease there is need for the greatest care not only in defining the results of observation but also in planning large-scale field and therapeutic experiments if they are to be most fruitful. To this end I would plead for the closest co-operation between the statistician and the clinician in this work. If this be achieved we shall hear less of the old gibe that "statistics may be made to tell anything, even the truth", and see fewer of those papers claiming, for a remedy in these diseases, 100% cures but written in that apologetic tone which is intended to convey that the author hopes to do better next time.

As an example of the tyranny of names and the absurd conclusions to which they may lead, let me quote, without acknowledgment for obvious reasons, a table from a recent paper, with the names of the collieries omitted.

Type of rheumatic ailment	Colliery A	B	C	Total
Rheumatoid arthritis..	8	5	9	22
Lumbago	5	10	13	28
Fibrositis	31	17	Nil	48
Sciatica	Nil	2	11	13
Neuritis	Nil	Nil	2	2

From an analysis of these figures which do not even specify the number of miners employed at each colliery so that an absolute and not a relative incidence alone can be seen, and without any diagnostic criteria for his differentiation of, for example, lumbago and fibrositis, the author concludes that as "there has not been observed a single case of fibrositis during the period of three months under review at Colliery C (the largest of the three)" this "surprising fact can be due to one thing only: Colliery C has pithead baths and the others have not". "This", he states, "is a striking illustration of the great medical value of such baths." But

assuming that, by a diagnostic talent vouchsafed to a select few only, he is able to differentiate between lumbago and fibrositis, what of the eleven cases of sciatica at Colliery C and their complete absence at A; and what of the greater incidence of lumbago at C? Would it not be just as tenable to infer that the pithead baths at C increased significantly the tendency there to sciatica and lumbago?

NOMENCLATURE AND CLASSIFICATION

To such a pass are we brought when we juggle with names. Yet it is impossible to speak of the objects of our study or to think clearly about them unless we give them names, and it is impossible to examine their relationships to each other, and their places in the almost infinite and incredibly complex phenomena of disease, in short to handle them scientifically, without classifying them in a formal way. But names must be our servants not our masters, and we must realize that it is man, and not God, who classifies.

The names we give to disease vary in worth and implication. Some signify a symptom—a deviation from the normal, e.g. dyspnœa; others suggest the tissue from which the symptom is alleged to arise, e.g. neuralgia and myalgia; whilst still others specify the exact anatomical reference of a symptom, e.g. sciatica, brachial neuralgia. Others refer to disorders of bodily function, e.g. jaundice, glycosuria. Yet others give in their nomenclature the pathology underlying the disease, e.g. arthritis, tenosynovitis, bursitis, and where possible its cause, e.g. gonococcal arthritis. Some recognize the association of phenomena in a regular, recurring pattern, e.g. Reiter's disease. Many are based on unconfirmed hypotheses of causation, e.g. fibrositis, whilst others, e.g. rheumatism and gout, have sufficiently strong historical roots to have survived an outmoded humoral pathology and need, if they are to be useful, to be defined anew. Is it surprising that the many classifications of rheumatic disease which include names of such diverse import should have failed in their purpose? I would suggest at the outset that the only basis on which to found a valid classification of the rheumatic diseases is primarily *anatomical*, i.e. involvement of skeletal, articular and neuromuscular structures. To suggest that rheumatic disorders should be defined as "painful locomotor disorders of unknown ætiology" is to exclude from the rheumatic group such conditions as dysenteric arthritis and sciatica associated with a prolapsed intervertebral disc, and thus to ignore what is the basis of a useful classification, viz. an emphasis on similarities.

Such a widening of the group might well include conditions not usually regarded as rheumatic diseases, e.g. trichinous myositis, yet there can be no sound reason which excludes this and yet includes, as does the Royal College of Physicians classification, gonococcal arthritis. We must find a fresh starting-point which takes note of established fact and present-day views rather than of traditional lore. We should in our classification recognize rheumatic fever, with its distinctive features of age-incidence, cardiac and neural involvement, and its response to salicylates, even though its ætiology remains obscure. We shall note arthritis of known cause —infective, traumatic, metabolic, allergic, neuropathic, hæmophilic—and arthritis in which the primary cause is unknown, be it called rheumatoid, cryptogenic, non-specific or idiopathic. But a common name is no guarantee of a common ætiology, so we shall not think of the group, rheumatoid arthritis, as necessarily homogeneous and of like cause. The name will unmask our ignorance as well as our knowledge and we shall endeavour by accurate and detailed observation of these cases to provide material for a clinical analysis related to age, sex, heredity, occupation, housing, geography, climate, social and economic conditions, previous infection, pregnancy, endocrine disturbances, allergic factors and the like, and thus to isolate groups which from their natural history and similar pattern may with advantage be studied together. Osteoarthritis will then be recognized as a possible sequel of any form of arthritis as well as an apparently primary degenerative process consequent on age or vascular changes. If we are wise we shall eschew such terms in our clinical classification as fibrositis, neuritis, strains, adhesions, and their associates, appreciating that in the vast majority of cases they are the refuges of the diagnostically destitute when confronted with inexplicable pains and that a hypothetical pathology may mask a problem but never solve it. In formulating any scheme for the treatment of rheumatism we must recognize that the persistence of pains labelled fibrositic, neuritic and the like, call for the use of every necessary diagnostic aid. In one week recently, I met a neurofibroma of the cauda equina, a vertebral metastasis from a bronchial carcinoma, a primary ovarian carcinoma, a chronic perinephric abscess, a prolapsed intervertebral disc, and a spondylolisthesis, all of which had been treated for several months as lumbago, fibrositis, or sciatica. These illustrate the dangers of "surrendering judgment" to the "fascination of a name".

AVAILABLE FACILITIES FOR TREATMENT

I was led into this digression from my main theme because I wished to stress that if we seek not simply more accurate statistical data but also a better understanding of the rheumatic diseases we must clarify and define our nomenclature and amend our classifications. But our present knowledge, inadequate and faulty though it be, leaves no doubt about the extent of the provision which must be made if sufferers are to be given "all the advice and treatment and care which they may need in matters of personal health", which is the avowed objective of Government policy in the proposed National Health Service. It would be idle to suppose that this can be provided overnight, but a start must be made and plans formulated. Contrast the incidence of rheumatism with the available facilities for treatment and it will be seen that even on the most generous estimate the gap will take many years to bridge. Davidson and Duthie estimated that in the nine large voluntary hospitals of Scotland there were treated annually only 1,000 rheumatic in-patients and 5,000 out-patients. In this country there are almost certainly less than 1,000 beds (including the special hospitals at spas) for the treatment of rheumatic disease. At eight British spas the maximum total daily treatments which can be provided in an eight-hour day is 8,340. Yet the figures available suggest that on any day in this country there are tens of thousands who suffer from and need treatment for rheumatism.

PAST NEGLECT

Why has there been hitherto so flagrant a neglect of rheumatic disease?

In the first place, rheumatism is not one of the fatal diseases; it ranks fourteenth in the causes of death. It lacks the dramatic appeal of cancer, tuberculosis and heart disease which in a few months may cut off their victims at an early age. In the days when facilities for research and the provision of treatment depended on voluntary gifts, the more fatal diseases attracted the attention of the philanthropist. But any Government must view with grave concern the major cause of industrial invalidism and the present Minister of Health has declared that the Government "attach the utmost importance to the attack on the group of illnesses known as rheumatism".

Secondly, the treatment of arthritis is much less spectacular and less overtly rewarding than most other diseases. It is prolonged and often tedious to both patient and doctor, and even the most satisfactory treatment may leave the patient with impaired function and ungainly deformity. Moreover in this treatment there has in the past been absent, all too often, the necessary co-operation between physician, orthopædic surgeon, physiotherapist and various specialists whose team work is essential if maximum recovery is to be secured. Neglect by the competent has left the field widely open to the incompetent and the unbridled therapeutic enthusiast. Sufferers, many hopeless and others disappointed, have succumbed to the blandishments of the unorthodox. The law has permitted the sale of nostrums "guaranteed to cure" and these have survived because many rheumatic complaints tend to natural remissions, and most patients and many doctors fail to distinguish *propter* from *post*.

This neglect by physicians is seen not only in the inadequate equipment, facilities and personnel for treating rheumatism in our larger teaching and general hospitals but, more seriously, in the absence from the medical student's curriculum of any adequate experience of rheumatic disease. He may be able to recognize many advanced types quite accurately but his knowledge of the early manifestations and the natural course of, for example, the various forms of arthritis; of the potentialities of treatment, and of the place and value of orthopædic methods, physiotherapy, occupational therapy, rehabilitation, both physical and psychological, in the management of rheumatic disease, is a lamentable void.

Finally, research into rheumatism failed to attract the support of academic bodies, such as the Medical Research Council. Their view has been expressed by Mellanby: "Extensive *ad hoc* research on a disease like rheumatism, however important as a practical problem, is liable to be unprofitable until the master key of its ætiology, or some other essential fact has been disclosed. This master key is just as likely to be discovered by the use of the experimental method over a wide field, as by directly studying a disease in which the experimental method is hardly available." This apology for withholding support is, I suggest, unwarranted on two counts. First, clinical observation and investigation by known methods may yield many secrets if pursued by competent investigators along sound lines. The differentiation of typhoid and typhus and their virtual elimination by general hygienic measures long antedated the discovery of their specific causes. It cannot be too strongly urged, in view of the orientation of so many laboratory research workers in medicine, that a so-called specific or necessary cause of disease is not of itself a wholly sufficient cause, except in the rarest instances. There are many contributory factors. For example, in the United States Public Health Survey disability from rheumatic disease was observed to be two to three times as great in the lower income group as in the higher. Secondly, the discovery of a specific cause is not necessarily followed by the discovery of a specific remedy. Though over half a century has passed since the tubercle bacillus was found we still seek the specific remedy for tuberculosis, but whilst awaiting its advent we continue to achieve cure in a large number of vicitims by non-specific measures. And so it is with chronic arthritis. Medical treatment, the prevention and correction of deformities, physiotherapy, exercises, manipulations, and a host of other measures lead in an increasing number of cases, especially when applied early, to a satisfactory outcome. Are not enquiries into their mode of action, and field investigations into the influence of such conditions as climate, occupation, and social and economic factors, sufficiently important for medical science to merit support from specifically designated "medical research" organizations? Until quite recently those who direct their policy have not thought so. The considerations thus far outlined call for action in four directions: (1) Research into the problems of rheumatism; (2) planning a service which makes available to all who need it all necessary treatment; (3) stimulating, in students and practitioners, a greater interest in the scope and methods of diagnosis and treatment of rheumatic disease; and (4) making available opportunities for the training of those who wish to specialize in this field.

RESEARCH

Research must be encouraged and supported. Money must be forthcoming, for though money never solves problems it helps men to solve them. This research must be closely associated with Universities and Medical Schools and their hospitals. Not only its prestige but its need in men and material demand this liaison. Only in this way will the co-operation of other experts, e.g. biochemists, physicists, pathologists and bacteriologists, be secured at the highest level. Programmes of research will cover all aspects of rheumatism. They will include fundamental problems in bone, muscle and joint physiology and pathology; they will cover epidemiology, diagnosis, and therapy. Some will be pursued in the laboratory, others in the field, and yet others in the clinics, but most will need data derived from all these sources and demand the services of a team. Many major investigations can even now be defined; here are a few:—

(1) Accurate statistical studies on morbidity rates, both national and local; and more intensive local studies dealing with selected areas of adequate size (say 50,000 to 100,000) which vary in climate, geography, subsoil, social and economic factors, diet, dominant occupations, and other possibly significant ways. Such local surveys would be intimate and detailed studies needing the co-operation of family and works' doctors, hospitals and their staffs, and medical officers of health.

(2) Rheumatism as an industrial problem; its incidence in selected occupations, e.g. among miners, dockers, postmen. It is here that the most careful scrutiny of clinical data given on certificates is needed. Statistics hitherto available are vitiated by many factors which tended to increase "rheumatism" as a certified cause of illness. A doctor in a mining practice tells me that before the advent of the paid holiday in the coal trade the increase of purely symptomatic rheumatism at holiday seasons was a noticeable feature. Moreover, it is the non-objective rheumatic complaints—"myalgia", "muscular rheumatism", "fibrositis"—which form the bulk of the diagnoses on medical certificates given to men who wish to leave the coal-mining industry on medical grounds. What are the conditions which predispose to rheumatism in certain industries? In miners, for example, what is the influence in the mine of atmospheric humidity; of passing from return (warm) roadways to intake (cold) roadways; of cramped posture especially when working in the seams; of the strenuous nature of the work; and of deprivation of sunlight? What is the effect at the surface of waiting about in wet clothes for buses and cycling or walking home after strenuous work in wet and cold weather? How far do housing conditions in mining villages, faulty diet, and neglect of general health contribute to a miner's rheumatism? It cannot be said that there has been an adequate investigation into these alleged predisposing causes. Careful studies in prophylaxis need to be undertaken. The influence of personal and domestic hygiene should be examined, so also conditions at work—working hours, fatigue, psychological factors, the nature of the work—and the influence of rest periods, pithead baths and ultraviolet light treatments in mines and factories. Available statistics emanate almost entirely from enthusiasts who, having formed an opinion on the merits of a method of treatment, find their results support their preconceived views. I have noted one such example earlier. A warning on this count is found in Dr. Dora Colebrook's admirable report, issued recently by the Industrial Health Research Board, on "Artificial Sunlight Treatment in Industry: A Report of results of three trials—in an office, a factory and a coal-mine". It had been widely claimed that ultraviolet radiation has a general "tonic" effect and not only prevents and corrects minor conditions of ill-health but reduces the amount of absenteeism due to accidents, rheumatism, common colds and general ill-health. Dr. Colebrook's report is a clear and careful presentation of a large-scale inquiry into this important subject, which is a model for such controlled therapeutic experiments. It reveals that the general application of ultraviolet radiation in small dosage has none of the "tonic" effects attributed to it. The use of artificial sunlight in this field is not a prophylactic measure but simply a modern version of sun-worship.

(3) There are many fundamental aspects of the growth of articular, skeletal and neuromuscular tissues and their normal senescence which need elucidation. Metabolic, nutritional, allergic, circulatory and other changes in the rheumatic subject need probing. Experimental arthritis and its relation to human arthritis and virus studies must be tackled. The local metabolism of joint tissues, e.g. the respiration of articular cartilage, the permeability of the synovia in health and disease—all these and a host of other problems come to mind, and new ones present themselves with discoveries in other fields. An interesting example has recently been published [5]. It is known that rheumatic fever affects predominantly mesenchymal tissues whose principal substrate is hyaluronic acid. The enzyme, hyaluronidase (which is the "diffusion factor" derived from many organisms including hæmolytic streptococci, and many tissues, especially testis) is capable of hydrolysing hyaluronic acid thus decreasing the viscosity of the tissues and favouring the passage of liquids, exudates and pathogenic micro-organisms into them. These are the tissues forming the synovial membranes and connective tissues of the articulations. What is impressive and might be of great significance is first, that oral or intravenous sodium salicylate inhibits this spread by as much as 66%, the degree of inhibition varying according to the dose of salicylate given; and secondly, that in patients with acute rheumatic fever or in those who have previously had rheumatic fever, "unique reactions with enormous diffusion of the dye and local œdema" sometimes follow the intradermal injection of dye and hyaluronidase. It is too early to assess the significance of these observations but they are illuminating in that they offer for the first time a rational explanation of the action of salicylates in acute rheumatism and throw light on an enzyme system which is capable of producing profound and dramatic effects in special regions without direct bacterial invasion.

(4) Many clinical investigations need launching. I have already referred to the need for accurate and detailed clinical records in the hope that these will lead to a sounder regrouping of the rheumatic disorders. Each of you will be prepared to give a list of clinical inquiries which should be undertaken, e.g. a critical reassessment of the role in rheumatic diseases of focal sepsis, of allergy, of endocrinous disturbances and the influence of the menopause; of the effects of gold and related drugs; of radiological studies and so forth. Some of these have been started on a large scale and we may look forward to useful knowledge emerging from them. But before this Section I would crave especially for basic investigation into the modes of action and the effects of the methods of physical medicine—heat, light, hydrotherapy, radiotherapy, mechanotherapy, and the physical factors governing the clinical application of these measures. In this the association of clinician and physicist is essential. How fruitful this partnership may be is shown by the work carried out in the Nuffield Department of Clinical Medicine at Oxford under Professor Witts' direction.

From this recital of possible research topics covering many fields, but by no means exhaustive, can it not be inferred that many valuable enquiries can be conducted even in the absence of a "master key"? Fortunately all do not hold Mellanby's view and the generous grant by the Nuffield Foundation of £100,000 to the University of Manchester to establish a research centre is welcome evidence of a renewed interest in rheumatism; the appointment of Professor S. L. Baker as Pathological Director of this new research centre is a guarantee of its status. The Foundation is also offering research fellowships in rheumatism so that no young and competent enthusiast need be deterred, as he was in the past, from working in this field because of financial obstacles.

A SERVICE FOR THE NATION

In planning a service for rheumatic disease which shall form part of a National

Health Service we have to bear in mind: (1) The paramount need for accurate diagnosis; (2) the parallel pursuit of clinical and basic research into the problems of rheumatism especially prophylaxis; (3) the provision of staff, and hospital beds in which patients may remain if need be for months in order to ensure that all the necessary treatment can be given; (4) the setting-up of clinics near the homes of patients or near their places of employment where minor forms of rheumatism can be treated and where those who have earlier been hospitalized can continue physical therapy. Moreover, it is necessary to consider what immediate action is possible to improve existing facilities for the diagnosis and treatment of the rheumatic diseases and the long-term development of such facilities. The plan suggested for immediate action is similar in structure to that of the scheme which is envisaged as a permanent service, so that our long-term policy will develop naturally out of the interim schedule. It is in brief suggested that:

(1) The teaching hospitals and a number of major general hospitals shall act as diagnostic and research centres.

(2) Each of these centres will be linked on the one side with one or more out-patient clinics with adequate facilities for physical therapy of most forms, and on the other with a base hospital providing long-stay beds and all necessary medical and surgical treatment, including occupational therapy and rehabilitation, for the chronic patient.

(3) Each diagnostic centre will provide the short-stay beds for investigation (it is unlikely that circumstances will free hospital beds in the diagnostic centre for long-stay patients) and also an out-patient clinic, though where more convenient the patient may be referred to one of the associated clinics.

(4) Patients will be referred by their family doctor, or by a works' doctor after consultation with the family doctor, to out-patient clinics in the first instance. These clinics, appropriately staffed, can and will deal with most patients giving them the appropriate treatment. But where the diagnosis is in doubt or where, after a few weeks, treatment has failed to benefit, then the patient is to be referred to the associated diagnostic centre.

(5) Base hospitals will care for long-stay cases referred for treatment by associated diagnostic centres; some will have out-patient departments and they too will refer doubtful or intractable cases to an associated diagnostic centre.

These constituents of the service will form a functional unit. Their staffs will be able to follow the progress of a case wherever it may be. We believe that this scheme will show not only "how good and how pleasant" but also how profitable it is for brethren in arms against the evils of rheumatism to "dwell together in unity". Already in some parts of the country a skeleton service based on the plan here described has been inaugurated.

EDUCATIONAL NEEDS

I have earlier referred to the deficiencies of our undergraduate medical curriculum in the teaching of rheumatic disease, especially its early diagnosis and the potentialities of treatment. No one is better aware than myself of the overcrowding of the students' timetable and no one would more earnestly plead for its pruning, but I will say no more than that I hold strongly that the major cause of industrial invalidism deserves some attention even if it be at the expense of rarer and more exotic topics. As a past sinner, I am heartened to observe that increasing efforts are being made in some schools to correct the omissions of the past.

We need to interest the students so that later some may be attracted to this special field. Now that we have heard on the highest authority that the fullest facilities for the treatment of rheumatic disease are to be provided as

(3) There are many fundamental aspects of the growth of articular, skeletal and neuromuscular tissues and their normal senescence which need elucidation. Metabolic, nutritional, allergic, circulatory and other changes in the rheumatic subject need probing. Experimental arthritis and its relation to human arthritis and virus studies must be tackled. The local metabolism of joint tissues, e.g. the respiration of articular cartilage, the permeability of the synovia in health and disease—all these and a host of other problems come to mind, and new ones present themselves with discoveries in other fields. An interesting example has recently been published [5]. It is known that rheumatic fever affects predominantly mesenchymal tissues whose principal substrate is hyaluronic acid. The enzyme, hyaluronidase (which is the "diffusion factor" derived from many organisms including hæmolytic streptococci, and many tissues, especially testis) is capable of hydrolysing hyaluronic acid thus decreasing the viscosity of the tissues and favouring the passage of liquids, exudates and pathogenic micro-organisms into them. These are the tissues forming the synovial membranes and connective tissues of the articulations. What is impressive and might be of great significance is first, that oral or intravenous sodium salicylate inhibits this spread by as much as 66%, the degree of inhibition varying according to the dose of salicylate given; and secondly, that in patients with acute rheumatic fever or in those who have previously had rheumatic fever, "unique reactions with enormous diffusion of the dye and local œdema" sometimes follow the intradermal injection of dye and hyaluronidase. It is too early to assess the significance of these observations but they are illuminating in that they offer for the first time a rational explanation of the action of salicylates in acute rheumatism and throw light on an enzyme system which is capable of producing profound and dramatic effects in special regions without direct bacterial invasion.

(4) Many clinical investigations need launching. I have already referred to the need for accurate and detailed clinical records in the hope that these will lead to a sounder regrouping of the rheumatic disorders. Each of you will be prepared to give a list of clinical inquiries which should be undertaken, e.g. a critical reassessment of the role in rheumatic diseases of focal sepsis, of allergy, of endocrinous disturbances and the influence of the menopause; of the effects of gold and related drugs; of radiological studies and so forth. Some of these have been started on a large scale and we may look forward to useful knowledge emerging from them. But before this Section I would crave especially for basic investigation into the modes of action and the effects of the methods of physical medicine—heat, light, hydrotherapy, radiotherapy, mechanotherapy, and the physical factors governing the clinical application of these measures. In this the association of clinician and physicist is essential. How fruitful this partnership may be is shown by the work carried out in the Nuffield Department of Clinical Medicine at Oxford under Professor Witts' direction.

From this recital of possible research topics covering many fields, but by no means exhaustive, can it not be inferred that many valuable enquiries can be conducted even in the absence of a "master key"? Fortunately all do not hold Mellanby's view and the generous grant by the Nuffield Foundation of £100,000 to the University of Manchester to establish a research centre is welcome evidence of a renewed interest in rheumatism; the appointment of Professor S. L. Baker as Pathological Director of this new research centre is a guarantee of its status. The Foundation is also offering research fellowships in rheumatism so that no young and competent enthusiast need be deterred, as he was in the past, from working in this field because of financial obstacles.

A SERVICE FOR THE NATION

In planning a service for rheumatic disease which shall form part of a National

Section of the History of Medicine

President—Sir ARTHUR MACNALTY, K.C.B., M.D.

[*January* 8, 1947]

Clinical Science in the Light of History

By A. P. CAWADIAS, O.B.E., M.D., F.R.C.P.

MEDICINE is an Art, and as such has existed since the beginnings of humanity. The Greeks, who created Science in that century tremendous in the development of humanity, the seventh century B.C., introduced as basis of the art or practice of medicine the scientific knowledge embodied in two sciences, Physiology in its wider sense, that is, Physio-pathology, and Clinical Science.

PHYSIO-PATHOLOGY AND CLINICAL SCIENCE

The object of Physiology in its wide sense, or Physio-pathology, is study of the functions of the human body, of the deviations of these functions, and of the action of various agents on these functions in their normal and their diseased state. It thus includes physiology proper, pathology, pharmacology and general therapy. Its method is *a priori* thinking, hypothesis, experimentation for the control of hypothesis, and reasoning on the basis of experimental facts towards the discovery of general laws concerning health and disease. In his reasoning the Physio-pathologist takes into consideration the facts of clinical observation, of Clinical Science. Pathology is thus a branch of physiology, and as this is the section of Physiology in closest contact with medicine I shall use indifferently the terms Physio-pathology and Pathology.

The object of Clinical Science is study of the morbid phenomena exhibited by human beings. Its method is clinical observation of these phenomena, their classification into morbid categories or diseases, and reasoning on the basis of clinical observation for discovery of methods of diagnosis and treatment of patients showing these particular morbid categories or diseases. In his reasoning the Clinical Scientist takes into consideration the data of Physio-pathology.

This science was known by the more general term *ἰητρική* translated into "Medicine". Sydenham introduced the more accurate and expressive term "Natural History of Diseases". Later the terms "Nosology" and "Clinical Medicine" were used. I do not know who first used the term Clinical Science, but I find it in the work of Sir James Paget and later in that of Knud Faber. It is to Sir Thomas Lewis, however, that we owe the general use of the term Clinical Science. Unfortunately, this great physician over-emphasized what I shall call later the "pathogenic chapter" of the natural history of diseases, and stressed certain clinical experimental procedures to which he seemingly attributed greater scientific status than to the great and real method of Clinical Science, namely, clinical observation. Neither can I accept his division into "Theoretical Medicine" and "Curative Medicine". There are only two divisions in medicine as a science, Physio-pathology and Clinical Science. We must therefore take the term "Clinical Science" in its traditional Sydenhamian sense of "Natural History of Diseases".

Although intimately connected—all sciences are connected—Pathology and Clinical Science are independent and separate sciences. Hippocrates in his *Ancient Medicine* had contrasted the *ἰητρική* with "Ὅτι Ἐμπεδοκλῆς ἢ ἄλλοι οἵ περί φύσεως γεγράφασι" (Empedocles and others have written on Nature). This is shown not only by the difference in their primary object and in their method, but also by the history of their creation and development.

part of the proposed national health service any competent specialist in this field can face the future with equanimity. The training of such specialists has been given careful consideration by my committee. A sound discipline in general medicine and the possession of a higher qualification are essential passports to specialized training. This will comprise medical work in the rheumatic field, practice in the non-operative orthopædic techniques necessary in the treatment of rheumatism, a working knowledge of the methods and machines of physiotherapy and the practical applications of physical medicine, occupational therapy and rehabilitation. Visits to foreign centres should be encouraged. The reawakening of interest in physical methods of treatment during the war makes it certain that given financial support during training, and satisfactory prospects for practising after training is completed, the right type of practitioner in sufficient numbers will be attracted to this field.

In the title of this lecture, I referred to "a challenge and an opportunity". The challenge lies in the incidence of rheumatic disease, in our inadequate understanding of it and in our past neglect. The opportunity for facing afresh the problems which this challenge presents comes with the introduction of a health service which promises to every citizen the treatment appropriate to his needs. But the opportunity is also a heavy responsibility for medicine. I have sought in this Address to indicate how it may be shouldered. Even with present knowledge, limited though it be, if we had sufficient trained personnel, hospital beds, and treatment facilities we could substantially lessen the invalidism resulting from rheumatism. We are appreciating in medicine, more and more fully, the importance of team work; in the rheumatic diseases the members of the team are many but they must work as a unit. Research will extend the frontiers of our knowledge, and we must see to it that in the future administrative medicine will repent its shortcomings of the past and keep pace with advancing knowledge. Mr. Bevan said, fifteen months ago, concerning suggestions embodied in a report on physical medicine, that he hoped the responsible Minister would "not be given any peace till they were carried out". We accept the challenge and shall act on this Ministerial injunction for in so doing we shall seek again to justify what was written of our profession many decades ago—"In it are united the aims and aspirations of the best and noblest of mankind".

REFERENCES

1 Incidence of Rheumatic Diseases, Report 23. (1924) Ministry of Health Reports on Public Health and Medical Subjects. H.M. Stationery Office.

2 Chronic Rheumatic Disease. The Report of the Medical Advisory Committee (Scotland) (1945) Department of Health for Scotland. H.M. Stationery Office. (Quotes Davidson and Duthie.)

3 Preliminary Reports, The National Health Survey: 1935 to 1936, Sickness and Medical Care Series. Bulletins Nos. 1 to 6. U.S. Public Health Service. Washington, D.C.

4 EDSTRÖM. G. (1945) "Reumatismens Betydelse som Folksjukdom i Sverige", *Uppsala LäkFören. Förh.*, **51**, 337.

5 DRY, T. J., BUTT, H. R., and SCHEIFLEY, C. H. (1946) "The Effect of Oral Administration of Para-Amino-Benzoic Acid on the Concentration of Salicylates in the Blood", Preliminary Report, *Proc. Staff Mayo Clin.*, **21**, 497.

Section of the History of Medicine

President—Sir ARTHUR MACNALTY, K.C.B., M.D.

[*January* 8, 1947]

Clinical Science in the Light of History

By A. P. CAWADIAS, O.B.E., M.D., F.R.C.P.

MEDICINE is an Art, and as such has existed since the beginnings of humanity. The Greeks, who created Science in that century tremendous in the development of humanity, the seventh century B.C., introduced as basis of the art or practice of medicine the scientific knowledge embodied in two sciences, Physiology in its wider sense, that is, Physio-pathology, and Clinical Science.

PHYSIO-PATHOLOGY AND CLINICAL SCIENCE

The object of Physiology in its wide sense, or Physio-pathology, is study of the functions of the human body, of the deviations of these functions, and of the action of various agents on these functions in their normal and their diseased state. It thus includes physiology proper, pathology, pharmacology and general therapy. Its method is *a priori* thinking, hypothesis, experimentation for the control of hypothesis, and reasoning on the basis of experimental facts towards the discovery of general laws concerning health and disease. In his reasoning the Physio-pathologist takes into consideration the facts of clinical observation, of Clinical Science. Pathology is thus a branch of physiology, and as this is the section of Physiology in closest contact with medicine I shall use indifferently the terms Physio-pathology and Pathology.

The object of Clinical Science is study of the morbid phenomena exhibited by human beings. Its method is clinical observation of these phenomena, their classification into morbid categories or diseases, and reasoning on the basis of clinical observation for discovery of methods of diagnosis and treatment of patients showing these particular morbid categories or diseases. In his reasoning the Clinical Scientist takes into consideration the data of Physio-pathology.

This science was known by the more general term *ἰητρική* translated into ‘‘Medicine’’. Sydenham introduced the more accurate and expressive term ‘‘Natural History of Diseases’’. Later the terms ‘‘Nosology’’ and ‘‘Clinical Medicine’’ were used. I do not know who first used the term Clinical Science, but I find it in the work of Sir James Paget and later in that of Knud Faber. It is to Sir Thomas Lewis, however, that we owe the general use of the term Clinical Science. Unfortunately, this great physician over-emphasized what I shall call later the ‘‘pathogenic chapter’’ of the natural history of diseases, and stressed certain clinical experimental procedures to which he seemingly attributed greater scientific status than to the great and real method of Clinical Science, namely, clinical observation. Neither can I accept his division into ‘‘Theoretical Medicine’’ and ‘‘Curative Medicine’’. There are only two divisions in medicine as a science, Physio-pathology and Clinical Science. We must therefore take the term ‘‘Clinical Science’’ in its traditional Sydenhamian sense of ‘‘Natural History of Diseases’’.

Although intimately connected—all sciences are connected—Pathology and Clinical Science are independent and separate sciences. Hippocrates in his *Ancient Medicine* had contrasted the *ἰητρική* with ‘‘‘Οτι ’Εμπεδοκλῆς ἤ ἄλλοι οἵ περί φύσεως γεγράφασι’’ (Empedocles and others have written on Nature). This is shown not only by the difference in their primary object and in their method, but also by the history of their creation and development.

Physio-pathology was created in the sixth century B.C. The first scientists, the Ionian Greeks, were designated Physiologists, meaning students of Nature in general. They were the first to reject the supernatural explanation of the universe current amongst the ancient Eastern peoples, and showed that all phenomena had a "natural explanation" and that the secrets of the world could be penetrated by the unprejudiced observation of things and the power of reason. When Pythagoras brought the torch of the Ionian Physiology to the Italo-Sicilian Greeks in the late sixth and early fifth centuries B.C., a group of physiologists passed from consideration of Nature in general to that of animal and principally human nature, and since then the term Physiology has been restricted to the study of the functions of the human body. The originators of this movement, apart from Pythagoras, were Alcmeon of Croton, Empedocles of Agrigentum, Diogenes of Apollonia, Hippon and Anaxagoras. From its inception Physiology was Physio-pathology, these first physiologists studying the functions of the human body in health and disease, as shown in the conception of disease expressed in the works of Alcmeon, Empedocles and Diogenes. In fact these first Physio-pathologists were the first physicians. The intimate union between Physiology and Pathology has persisted ever since. It was developed in the work of Galen, the greatest of the Greek Physio-pathologists. It was codified later through the work of John Hunter, Magendie and Claude Bernard, and is embodied in Magendie's famous dictum, "Medicine (meaning pathology) is the physiology of the diseased individual".

The method adopted by the first physiologists was *a priori* reasoning and observation, including dissections. Experimentation was introduced by the Alexandrians of the third century B.C. and principally by Galen, but received its greatest impetus from Harvey, who thus revived Physio-pathology as his contemporary, Sydenham, revived Clinical Science. Since Harvey the basic method of Physio-pathology has been experimentation.

Clinical Science was introduced a little later, in fact in the fifth century, by the Coan physicians represented by Hippocrates, by the Cnidians represented by Euryphon and also by the physicians of Rhodes. The islands of Cos and Rhodes and the peninsula of Cnidos were colonized by that most virile section of the Greek people, the Dorians, who were, however, influenced by the neighbouring Ionia and also by East Asia. Asclepios, the God of Medicine, was one of the chief Dorian gods, and from the Dorian peninsula of Peloponnesus with its great sanctuary of Asclepios at Epidauros, this cult was brought to Cos, Cnidos and Rhodes. The priests of Asclepios, the Asclepiadæ, formed a princely priest-family which attributed its origin to Podalirios, son of Asclepios. The Asclepiadæ did not continue in their purely priestly caste spirit. They were not Egyptians, they were Greeks. Just as the Ionians had detached themselves from the magic and supernatural explanations of the universe and interpreted Nature through natural laws, the Coan and Cnidian Asclepiadæ abandoned purely religious healing rites and, with the object of giving more effective help to the patients who sought relief in the temples of Asclepios, they adopted clinical observation and healing on the basis of clinical observation.

THE METHOD OF CLINICAL SCIENCE

The method of Hippocrates, the founder of Clinical Science, consists, as described by Plato, in careful analysis of nature (*Διελέσθαι τήν φύσιν* or clinical observation), in enumeration of its types (*ἀριθμήσασθαι τά εἴδη* or nosographical classification), and in definition of the appropriate treatment for each (*προσαρμόττειν ἕκαστον ἑκάστῳ*).

The Egyptians also observed and recorded observations of their patients, but clinical observation as introduced by the Coans and Cnidians is an active critical observation demanding not only keen sense but also a special intellectual structure. The heights attained by this method among the ancient Greeks can be gathered from what we know of the Empiricists and particularly from the book of *Sextus Empiricus*, which is the *Novum Organum* of the ancient Greek clinicians. The Empiricists built their clinical science on their famous tripod *ἱστορία* (observation of others), *τήρησις* (observation of the physician himself), and *ἀπό τοῦ ὁμοίου ἀκολουθία* (conclusion from the similarities of both). This special method of clinical observation has penetrated subconsciously into our own work, and we forget the painful steps through which it was elaborated, just as we forget that our mode of thought in general derives from the clear logic constructed by the ancient Greeks, and for this reason our mode of thought differs from that of certain peoples such as the Far Eastern peoples, who have not so far come under Hellenic influence.

It is difficult to go through *Sextus Empiricus* and the passages from Hippocrates and Galen relating to the method of clinical observation, but nearer to us there is a remarkable treatise on clinical observation, the *On Experience in Medicine* of Johann Georg Zimmermann (1728-1795), a Swiss physician at the Court of Hanover. This work, inspired by study of the Greek works and often read by the French clinicians of the nineteenth century, deserves more popularity amongst us. The following definition is from that work. "Observation is an aptitude for seeing an object in its true light and distinguishing what there is in it more or less useful. . . . It is nothing more than the conception of the affinity of things and of the signs which point out to us their order and combination. The perception of our senses would be of little use if the mind remained in a state of inactivity. The soul would be rich in images but very barren in ideas. We are obliged to have a certain activity of mind whenever we see—and in this there is an element of comparison."

Thus, what we call clinical observation, as codified by the ancient Greek clinical scientists, is a complicated process and consists of far more than merely "seeing" and noting what falls before our senses. It consists in the perception of apparent and hidden symptoms (thus in perception of biochemical disturbances, for example) and principally in comparison and synthesis into an all-embracing "intuition" of the totality of symptoms. It is thus a far more complex and active procedure than physiological experiment. The term "observation" is up to a certain point a misnomer. Clinical observation is more than observation.

Connected with clinical observation, and indispensably united with it in the mind of the clinical scientist, is nosological thinking. The clinician classifies his observations into special categories, "diseases". He constructs such diseases, or he enters his observations into "diseases" already described. This nosological thinking was also introduced by the Coans and the Cnidians, who saw that the morbid phenomena exhibited by patients are of immense variety and that for their study a method of classification was necessary. They arrived at that method of classification by observing that certain symptoms occurred in patients in a certain regularity of combination and development. They abstracted these combinations of morbid phenomena from the individual and constructed special categories, "diseases". The Coan and Cnidian Asclepiadæ thus introduced into science in general the conception of the εἶδος or type by abstracting essential features, and this conception of type has helped enormously the development of all sciences.

A subsidiary process in the development of clinical science consists in a special utilization of the findings of pathology. Pathology (physio-pathology) and Clinical Science have always been intimately connected. As already stated, the early Egyptians also made clinical observations, and these physicians had little to learn about specialization and empirical observation but were unable to build a clinical science. The Coan and Cnidian Asclepiadæ achieved this because they had learned from the Ionian Physiologists how to look for universal laws that could create a theoretical system capable of upholding a real scientific movement. As Professor Jaeger puts it (*Paedia*, p. 20): "Truth can never be dissolved into the infinite variety of individual cases; or if it could it would have no real meaning for us."

Physio-pathology was created in the sixth century B.C. The first scientists, the Ionian Greeks, were designated Physiologists, meaning students of Nature in general. They were the first to reject the supernatural explanation of the universe current amongst the ancient Eastern peoples, and showed that all phenomena had a "natural explanation" and that the secrets of the world could be penetrated by the unprejudiced observation of things and the power of reason. When Pythagoras brought the torch of the Ionian Physiology to the Italo-Sicilian Greeks in the late sixth and early fifth centuries B.C., a group of physiologists passed from consideration of Nature in general to that of animal and principally human nature, and since then the term Physiology has been restricted to the study of the functions of the human body. The originators of this movement, apart from Pythagoras, were Alcmeon of Croton, Empedocles of Agrigentum, Diogenes of Apollonia, Hippon and Anaxagoras. From its inception Physiology was Physio-pathology, these first physiologists studying the functions of the human body in health and disease, as shown in the conception of disease expressed in the works of Alcmeon, Empedocles and Diogenes. In fact these first Physio-pathologists were the first physicians. The intimate union between Physiology and Pathology has persisted ever since. It was developed in the work of Galen, the greatest of the Greek Physio-pathologists. It was codified later through the work of John Hunter, Magendie and Claude Bernard, and is embodied in Magendie's famous dictum, "Medicine (meaning pathology) is the physiology of the diseased individual".

The method adopted by the first physiologists was *a priori* reasoning and observation, including dissections. Experimentation was introduced by the Alexandrians of the third century B.C. and principally by Galen, but received its greatest impetus from Harvey, who thus revived Physio-pathology as his contemporary, Sydenham, revived Clinical Science. Since Harvey the basic method of Physio-pathology has been experimentation.

Clinical Science was introduced a little later, in fact in the fifth century, by the Coan physicians represented by Hippocrates, by the Cnidians represented by Euryphon and also by the physicians of Rhodes. The islands of Cos and Rhodes and the peninsula of Cnidos were colonized by that most virile section of the Greek people, the Dorians, who were, however, influenced by the neighbouring Ionia and also by East Asia. Asclepios, the God of Medicine, was one of the chief Dorian gods, and from the Dorian peninsula of Peloponnesus with its great sanctuary of Asclepios at Epidauros, this cult was brought to Cos, Cnidos and Rhodes. The priests of Asclepios, the Asclepiadæ, formed a princely priest-family which attributed its origin to Podalirios, son of Asclepios. The Asclepiadæ did not continue in their purely priestly caste spirit. They were not Egyptians, they were Greeks. Just as the Ionians had detached themselves from the magic and supernatural explanations of the universe and interpreted Nature through natural laws, the Coan and Cnidian Asclepiadæ abandoned purely religious healing rites and, with the object of giving more effective help to the patients who sought relief in the temples of Asclepios, they adopted clinical observation and healing on the basis of clinical observation.

THE METHOD OF CLINICAL SCIENCE

The method of Hippocrates, the founder of Clinical Science, consists, as described by Plato, in careful analysis of nature (*Διελέσθαι τήν φύσιν* or clinical observation), in enumeration of its types (*ἀριθμήσασθαι τά εἴδη* or nosographical classification), and in definition of the appropriate treatment for each (*προσαρμόττειν ἕκαστον ἑκάστῳ*).

The Egyptians also observed and recorded observations of their patients, but clinical observation as introduced by the Coans and Cnidians is an active critical observation demanding not only keen sense but also a special intellectual structure. The heights attained by this method among the ancient Greeks can be gathered from what we know of the Empiricists and particularly from the book of *Sextus Empiricus*, which is the *Novum Organum* of the ancient Greek clinicians. The Empiricists built their clinical science on their famous tripod *ίστορία* (observation of others), *τήρησις* (observation of the physician himself), and *ἀπό τοῦ όμοίου ἀκολουθία* (conclusion from the similarities of both). This special method of clinical observation has penetrated subconsciously into our own work, and we forget the painful steps through which it was elaborated, just as we forget that our mode of thought in general derives from the clear logic constructed by the ancient Greeks, and for this reason our mode of thought differs from that of certain peoples such as the Far Eastern peoples, who have not so far come under Hellenic influence.

It is difficult to go through *Sextus Empiricus* and the passages from Hippocrates and Galen relating to the method of clinical observation, but nearer to us there is a remarkable treatise on clinical observation, the *On Experience in Medicine* of Johann Georg Zimmermann (1728-1795), a Swiss physician at the Court of Hanover. This work, inspired by study of the Greek works and often read by the French clinicians of the nineteenth century, deserves more popularity amongst us. The following definition is from that work. "Observation is an aptitude for seeing an object in its true light and distinguishing what there is in it more or less useful. . . . It is nothing more than the conception of the affinity of things and of the signs which point out to us their order and combination. The perception of our senses would be of little use if the mind remained in a state of inactivity. The soul would be rich in images but very barren in ideas. We are obliged to have a certain activity of mind whenever we see—and in this there is an element of comparison."

Thus, what we call clinical observation, as codified by the ancient Greek clinical scientists, is a complicated process and consists of far more than merely "seeing" and noting what falls before our senses. It consists in the perception of apparent and hidden symptoms (thus in perception of biochemical disturbances, for example) and principally in comparison and synthesis into an all-embracing "intuition" of the totality of symptoms. It is thus a far more complex and active procedure than physiological experiment. The term "observation" is up to a certain point a misnomer. Clinical observation is more than observation.

Connected with clinical observation, and indispensably united with it in the mind of the clinical scientist, is nosological thinking. The clinician classifies his observations into special categories, "diseases". He constructs such diseases, or he enters his observations into "diseases" already described. This nosological thinking was also introduced by the Coans and the Cnidians, who saw that the morbid phenomena exhibited by patients are of immense variety and that for their study a method of classification was necessary. They arrived at that method of classification by observing that certain symptoms occurred in patients in a certain regularity of combination and development. They abstracted these combinations of morbid phenomena from the individual and constructed special categories, "diseases". The Coan and Cnidian Asclepiadæ thus introduced into science in general the conception of the εἶδος or type by abstracting essential features, and this conception of type has helped enormously the development of all sciences.

A subsidiary process in the development of clinical science consists in a special utilization of the findings of pathology. Pathology (physio-pathology) and Clinical Science have always been intimately connected. As already stated, the early Egyptians also made clinical observations, and these physicians had little to learn about specialization and empirical observation but were unable to build a clinical science. The Coan and Cnidian Asclepiadæ achieved this because they had learned from the Ionian Physiologists how to look for universal laws that could create a theoretical system capable of upholding a real scientific movement. As Professor Jaeger puts it (*Paedia*, p. 20): "Truth can never be dissolved into the infinite variety of individual cases; or if it could it would have no real meaning for us."

The Pathologist has to take the findings of Clinical Science into consideration and the Clinical Scientist is indebted to progress in knowledge of his diseases to the findings of Pathology. However, the Clinical Scientist must utilize pathological findings in the light of his method of clinical observation and nosographical classification. He cannot take pathological findings uncritically and deduce from them clinical scientific principles. Pathology helps but cannot dominate Clinical Science. Whenever it has attempted to dominate, the result has been disastrous. This was recognized by Hippocrates, who in his *Ancient Medicine* pointed out the danger of domination of *ἰητρική* (what we to-day call clinical science) by the Ionian Physio-pathology. Two examples from recent history confirm this opinion of Hippocrates.

On the basis of the clinical scientific method of observation (clinico-anatomical), Laennec had shown the similar nature of tubercles, caseiform processes and cavities. Virchow and his pupil Niemeyer, on the basis of pure pathology, separated these processes and embarked on speculation about chronic catarrhal pneumonia, caseous and destructive phthisis and so on, until the discoveries of Villemin and Koch proved them wrong and the despised "ontologist" Laennec right. Bretonneau, also on the basis of clinico-anatomical observation, identified pharyngeal diphtheria and croup. With Teutonic dogmatism Virchow declared them to be separate and started semi-metaphysical speculations on diphtheria and croupous inflammation. Of course, Bretonneau was shown to be right. This does not imply criticism of the general work of Virchow and his pupils. Virchow did much for Pathology, but he had no understanding of Clinical Science and by attempting to suppress it he gave to German in contrast to British and French medicine an un-Hippocratic theoretical and unclinical spirit which has persisted until to-day.

THE IMPORTANCE OF CLINICAL SCIENCE

From the beginning certain arguments were directed against the nosographical method of Clinical Science. They were stated and answered by Hippocrates himself. They were shown to arise from confusion between the science of medicine (clinical science) and the art of medicine. Diseases are artificial constructions, but necessary for the classification of knowledge, and thus necessary as far as scientific method is concerned. In practice, in art we deal not with diseases but with individual patients. Our object is not to place our patient into a certain morbid category; this is only a useful preliminary measure. Our object is to study the individual patient and discover what is wrong with his physiology (and psychology) and what has caused his individual disturbances. With this aim we study the history of the individual, the mode of function of his various organs and systems including the psyche, the immediate ætiological conditions which have brought about these disturbances, the special heredity, environment and constitution. To do all this, however, we must possess the science of the morbid phenomena as exhibited by human patients. We must possess Clinical Science, and Clinical Science cannot be taught, cannot develop, except in terms of morbid categories.

There are no diseases but only individual patients. This platitude has often been reiterated, and everybody agrees with it. We cannot, however, approach the individual patient without previous knowledge of diseases. Clinical Science is based on artificial constructions. This also is true, but all sciences are artificial. The important point is whether this artifice works. And history shows that it works. All physicians who have attempted to practise on the basis of Pathology alone, all those who have endeavoured to bypass Clinical Science, have failed. Such was the lot of the λογικοί (rationalists) who came after Hippocrates, of the pneumatists, the methodists and other dogmatists of Alexandrian and Roman times, of the scholastics of the Middle Ages, of the iatrochemists and iatrophysicists of the sixteenth, seventeenth and eighteenth centuries, the animists and vitalists and Brownians of the eighteenth century, of the disciples of Rasori, of Broussais and the early disciples of

Hahnemann in the early nineteenth century, and of the followers of the German so-called physiological school of the mid-nineteenth century. To enumerate all these schools, to remember all these names, is to give a list of the medical errors of the past. The practice of all these schools, based on purely pathological conceptions, resulted in one-sided, often violent and always ineffective treatments.

Nearer to our own times, what happened to the German school of physiological or rational medicine is a potent illustration. The Germans came late into medicine. They had not the advantage of the earlier infiltration of Hippocratic ideas enjoyed by Italy, Great Britain and France. The attempt of Schönlein to introduce the French and British Clinical Science failed in great part. The Germans were too prone to speculation and were too dominated by the principles of "Natural Philosophy" to understand clear clinical scientific thinking. When, in the middle of the nineteenth century, they decided to build up a German medicine, they did not adopt the principles of Clinical Science but were seduced by the empty speculations of the "Physiological Medicine" of Broussais. They rejected nosographical classifications and tried to build up their practice on Physio-pathology alone. This was the tendency of Traube, of Wunderlich, of Virchow. The result was a great physiological and pathological work, but from the practical point of view a chaos of empty speculations and theories. This was realized by men like Pfeuffer (himself at the beginning a follower of the Physiological School), Frerichs, Leyden and Naunyn, who brought German medicine back into the fold of British and French Nosology.

In knowledge of disease as well as in practice Clinical Science is as important as Pathology. The mistaken conceptions of tuberculosis and of diphtheria reached by the Germans on the sole basis of pathology illustrate this point.

Thus history shows that it is not true to say that Pathology is a science and Clinical Medicine an art. Clinical Medicine is a science, Clinical Science, the natural history of diseases, a science indispensable in the theory and practice of medicine, a great science which introduced the first two real scientific methods, observation and typology.

ISOLATION AND CLASSIFICATION OF DISEASES

From the days of the Hippocratists and the Cnidians to the beginning of the nineteenth century, morbid categories or "diseases" were isolated on the basis of their clinical manifestations. Diseases were symptom complexes or, to use the term of the Empiricists, clinical syndromes. With the advent of the anatomo-clinical schools of the early nineteenth century many diseases were isolated on the basis of their clinical manifestations connected with particular anatomical lesions. These diseases were thus clinico-anatomical syndromes. Later, some diseases were isolated on the basis of clinical manifestations connected with a particular physio-pathological disturbance or with a specific causal factor.

A mode of classification of diseases was necessary for scientific progress. Apart from a rudimentary attempt at classification found in the Cnidian work and based on the localization of diseases, the first real attempt at classification was made by François Boissier de Sauvages of Montpellier in 1731. Sauvages was influenced by the work of Sydenham, and essayed a classification of diseases on the principle of classification of natural history. He was not only a physician, but also a botanist and a friend of Charles Linné. He based his classification exclusively on symptomatological pictures and grouped diseases in classes, orders and genera just as natural scientists at that time were arranging plants and animals. The classification of Sauvages was cumbersome but it represented a first attempt at putting knowledge in order. William Cullen gave a better classification in his Nosology (1769). Whereas Sauvages often labelled isolated symptoms as "diseases", Cullen grouped symptoms into symptom complexes. This was more on the lines of the Hippocratists, the Cnidians and of Sydenham. Nosology was thus simplified, and the number of species of diseases or morbid categories was reduced. However, Cullen's nosological divisions, like those of Sauvages, were based only on symptoms. A further advance was marked by Philippe Pinel, whose *Nosographie Philosophique* was published in 1798. His classification was based on anatomical and physiological considerations.

Since Pinel nosologies, that is, systematic expositions of diseases, have developed better systems of classification but a perfect classification has not been found and is in fact impossible. We have to catalogue and group morbid categories constructed on various principles. Some diseases are isolated on the basis of their clinico-anatomical picture, others on the basis of their particular ætiology, others on the basis of their special physio-pathology, others on the basis of the purely clinical picture. Thus each arrangement has its defects and exhibits only some forced approximation. We have to consider it as a repertory lacking complete exactitude, and select that which brings together the greatest number of analogous diseases. We have also to remember that the classification of diseases is secondary, the most inportant thing being the isolation of diseases, the accurate description of their specific combination of symptoms and of their specific course.

The systematic exposition of diseases, thus the systematic exposition of Clinical Science, would have been designated "Natural History of Diseases" by Sydenham. Sauvages, Cullen, Pinel and the French clinicians of the first half of the nineteenth century termed their expositions Nosologies, a term maintained in modern Greek medical terminology. In contemporary France and in German-speaking countries the term "special pathology" is current, a term which may cause confusion with Pathology, which is a branch of Physiology. In English-speaking countries the term Practice of Medicine is used, meaning "Introduction" in the Oslerian sense to the practice of medicine. The term Clinical Science would be more appropriate.

THE CLINICAL DESCRIPTIVE CHAPTER IN THE NATURAL HISTORY OF DISEASES

The clinical descriptive chapter is the basic chapter in the natural history of diseases. It allows isolation of the particular disease and forms the frame for pathogenic, ætiological, prognostic and therapeutic considerations.

(1) The first clinical scientists described the signs and symptoms in diseases. Endowed with great powers of observation and the directness of vision characteristic of the ancient Greeks, they often gave descriptions which have never been surpassed. The Hippocratists dwelt on general symptoms. The Cnidians endeavoured to study local symptoms pointing to disease of a particular organ. With the Empiricists study of the symptoms of particular "disease types" reached its zenith. A great contribution to the symptomatological picture of diseases was made by the Neo-Hippocratists of the first century of our era, Archigenes of Apamia, Aretaios and Soranos. Symptomatological and semiological description reached its peak in the work of Sydenham, whose observational and critical powers and searching vision appear to me as similar to those of Hippocrates.

Work has proceeded on these lines during the course of the centuries, and the symptomatological-semiological picture has been progressively completed. The ancient Greeks dwelt on symptoms, although signs elicited by auscultation, percussion and palpation were mentioned in the Hippocratic writings. With the advent of the anatomo-clinical school, signs were much more developed and helped to complete the clinical pictures of known diseases and to isolate new ones. Recently signs elicited by special explorations such as the various endoscopies and radiology have been added.

(2) A further step in the descriptive chapter of the natural history of diseases was completion of the disease picture through consideration of the anatomical lesions connected with the symptoms and signs.

The first clinical scientist to connect a symptomatological picture with an anatomical lesion was Erasistratos, who flourished in the third century B.C. in Antioch as Court physician to the Selencidæ, and in Alexandria. He adopted the principles of the Cnidian school and looked for the " seats of diseases", *Οὐ μόνον τό πάθος ὁποῖον ἐστίν ἀλλά καί τόν πάσχοντα τόπον.* In the brilliant Alexandria of the first two Ptolemies dissection of humans was permitted, and Erasistratos availed himself of these opportunities. He found that in dropsical patients the liver was hard as stone. He described lesions of the liver and intestine in a form of snakebite, and deduced from his post-mortem examinations the seat of pleuritis.

During the Renaissance Francis Bacon in his *Advancement of Learning* pointed out the two chief ways in which he thought medicine might advance: In the first place he advocated revival of the Hippocratic method of recording cases in order that through such observations the description of diseases which had been undertaken in ancient Greek medicine might be amplified and extended. In the second place, he held that through anatomical investigation the pathological changes, "the footsteps of diseases", should be studied, and findings compared with the symptoms during life. But on the latter point neither the lead of Erasistratos nor the opinion of Bacon was followed for centuries. It is true that physicians made post-mortems, and a few of them like the Dane, Thomas Bartholin (1616-1680), and Theophilus Bonetus (1621-1689) published collections of anatomo-clinical observations, but they did not endeavour to apply the anatomical findings to complete the pictures of diseases.

In 1761 Morgagni published his *De Sedibus et Causis Morborum per Anatome Indagati*, in which he followed the Hippocratic lines of describing diseases but added anatomical findings to the Hippocratic symptoms and signs. He thus showed that disease pictures can gain in completeness and precision by addition to the symptomatological-semiological picture of the corresponding anatomical lesion.

Xavier Bichat in 1801 went a step further. Whereas Morgagni emphasized the lesions of whole organs Bichat showed that the morbid changes in an organ can be dissociated in various tissues each of which follows a different course. Later Rudolf Virchow (1821-1902), availing himself of modern techniques, discovered the importance of cellular lesions. Following the lead of the Morgagni-Bichat-Virchow triumvirate, clinical scientists completed their disease pictures by linking their symptomatological-semiological pictures with the macroscopic and microscopic anatomical pictures. Thus known diseases were more completely described and many new ones were isolated. Morbid anatomy gave to Clinical Science and thus to medicine a greater scientific status.

The first work following the lead of Morgagni was, I think, that of Mathew Baillie, who in 1793 published the first book describing the anatomical lesions in various diseases. Unfortunately Baillie, submerged by his enormous practice, lacked the time to give a powerful impetus to this new method of Clinical Science. This was reserved for Napoleon's famous physician, Corvisart. In his *Essai sur les Maladies et les Lésions Organiques du Cœur* (1806) he maintained that disease could not bc considered as a mere grouping of symptoms, but that the study of anatomical lesions should complete the picture.

The new method of Clinical Science was followed by great clinicians in France and England whose names are familiar to all of us. Laennec, Bayle, Charcot, Bright, Hodgkin, Addison, Graves and many others worked on the Coan-Cnidian lines, and the British in particular considered pathological anatomy as merely an aid to clinical medicine and subordinated anatomical findings to the general clinical picture of disease. Robert Graves (1796-1853) said in his clinical lectures that anatomical lesions had the rank of symptoms.

The Vienna school also adopted pathological anatomy, but not on Hippocratic lines. Skoda (1805-1881) and principally Rokitansky (1804-1878) subordinated pathological anatomy to clinical medicine. They placed anatomical alterations first in the classification and description of morbid processes and considered that the task diseases or morbid categories was reduced. However, Cullen's nosological divisions, like those of Sauvages, were based only on symptoms. A further advance was marked by Philippe Pinel, whose *Nosographie Philosophique* was published in 1798. His classification was based on anatomical and physiological considerations.

Since Pinel nosologies, that is, systematic expositions of diseases, have developed better systems of classification but a perfect classification has not been found and is in fact impossible. We have to catalogue and group morbid categories constructed on various principles. Some diseases are isolated on the basis of their clinico-anatomical picture, others on the basis of their particular ætiology, others on the basis of their special physio-pathology, others on the basis of the purely clinical picture. Thus each arrangement has its defects and exhibits only some forced approximation. We have to consider it as a repertory lacking complete exactitude, and select that which brings together the greatest number of analogous diseases. We have also to remember that the classification of diseases is secondary, the most inportant thing being the isolation of diseases, the accurate description of their specific combination of symptoms and of their specific course.

The systematic exposition of diseases, thus the systematic exposition of Clinical Science, would have been designated "Natural History of Diseases" by Sydenham. Sauvages, Cullen, Pinel and the French clinicians of the first half of the nineteenth century termed their expositions Nosologies, a term maintained in modern Greek medical terminology. In contemporary France and in German-speaking countries the term "special pathology" is current, a term which may cause confusion with Pathology, which is a branch of Physiology. In English-speaking countries the term Practice of Medicine is used, meaning "Introduction" in the Oslerian sense to the practice of medicine. The term Clinical Science would be more appropriate.

THE CLINICAL DESCRIPTIVE CHAPTER IN THE NATURAL HISTORY OF DISEASES

The clinical descriptive chapter is the basic chapter in the natural history of diseases. It allows isolation of the particular disease and forms the frame for pathogenic, ætiological, prognostic and therapeutic considerations.

(1) The first clinical scientists described the signs and symptoms in diseases. Endowed with great powers of observation and the directness of vision characteristic of the ancient Greeks, they often gave descriptions which have never been surpassed. The Hippocratists dwelt on general symptoms. The Cnidians endeavoured to study local symptoms pointing to disease of a particular organ. With the Empiricists study of the symptoms of particular "disease types" reached its zenith. A great contribution to the symptomatological picture of diseases was made by the Neo-Hippocratists of the first century of our era, Archigenes of Apamia, Aretaios and Soranos. Symptomatological and semiological description reached its peak in the work of Sydenham, whose observational and critical powers and searching vision appear to me as similar to those of Hippocrates.

Work has proceeded on these lines during the course of the centuries, and the symptomatological-semiological picture has been progressively completed. The ancient Greeks dwelt on symptoms, although signs elicited by auscultation, percussion and palpation were mentioned in the Hippocratic writings. With the advent of the anatomo-clinical school, signs were much more developed and helped to complete the clinical pictures of known diseases and to isolate new ones. Recently signs elicited by special explorations such as the various endoscopies and radiology have been added.

(2) A further step in the descriptive chapter of the natural history of diseases was completion of the disease picture through consideration of the anatomical lesions connected with the symptoms and signs.

The first clinical scientist to connect a symptomatological picture with an anatomical lesion was Erasistratos, who flourished in the third century B.C. in Antioch as Court studied in the light of the whole clinical frame. This was effected chiefly by Albert Robin and by Fernand Widal.

Each disease thus represents a totality of symptoms, which are not only the subjective phenomena but include the so-called clinical signs and the signs given by special methods of exploration including laboratory exploration. Clinical observation means not only seeing but also arranging all these symptoms in their proper order of importance, and particularly in considering the course of this totality of symptoms. This descriptive chapter is the basis of Clinical Science. The description of a new disease and the rearrangement of the description of a known disease are of extremely great importance in practical medicine.

THE OTHER CHAPTERS OF THE NATURAL HISTORY OF DISEASES

The pathogenic chapter provides the answer to the question as to what kind of disturbances of body-mind function are the basis of the symptoms shown by a patient who enters into a particular disease type. The term physio-pathological chapter also is used, but I prefer the term pathogenic so as to avoid confusion with physio-pathology.

For construction of this chapter the clinical scientist has to take as main basis the data of Physio-pathology, but he has to consider these data in the light of his special method of clinical observation and, with the object of understanding the particular disease he is studying, he can resort to animal experimentation and to certain clinical tests. Thus, although related intimately with Physio-pathology, this chapter is not Physio-pathology. It is to Sir Thomas Lewis that we owe the codification of the method of constructing this particular chapter in the natural history of diseases. This chapter is not, however, as he tended to consider, the whole of Clinical Science but only a part, and as in Clinical Science in general the preponderant element is clinical observation, not experimentation.

The ætiological chapter describes the factors that have determined the disturbances in physiology manifested by symptoms in a patient showing a particular disease. The Hippocratists constructed this chapter on the basis of clinical observation, including a careful history, and described for every disease an interplay of external abnormal conditions—meteorological, traumatic, dietetic and psychological (the *κατάστασις* or external constitution), acting on a specially predisposed individual, on the *φύσις* or internal constitution. Sydenham developed this chapter on the same lines and had the intuition of specific infective ætiology. Physio-pathology helps clinical observation by its study of the various factors determining disease and of the mechanism of their action, but the last word remains with clinical observation. To the Hippocratic external factors physio-pathology has added the infective factors, and contemporary work as embodied in the teaching of Professor John Ryle, the social factors.

The therapeutic chapter was also introduced by the Hippocratists and the Cnidians on the basis of clinical observation. These clinicians applied medicines to patients entering into a special disease type on the basis of tradition or of certain theoretical physio-pathological considerations, and observed the effects of their remedies. A remedy which benefited a patient suffering from a known disease is likely to benefit another patient suffering from the same disease. This is the famous principle of *ἀπό τοῦ ὁμοίου ἀκολουθία*, the principle of the clinical empirical method. Sydenham worked on these lines to discover his specific remedies. Progress in Physio-pathology enabled clinicians to perfect this chapter. Study of therapeutic agents, pharmacology in its extended sense, is basically a branch of Physio-pathology, and further the more perfect conception of the pathogeny of various diseases attained by advances in general Physio-pathology allowed of more precise indications. However, the method of clinical observation has the last word. Whatever the physio-pathological conception, the clinical effect of remedies is over-riding in importance.

of clinical medicine was confined to demonstrating these anatomical changes in patients. Thus anatomical diagnosis became the sole object of the physician's efforts. They were far removed from the breadth of view of the natural history of diseases shown by Hippocrates and Sydenham. The medicine of Skoda and of Rokitansky was really a mortuary medicine. That the principle was wrong is shown by the therapeutic nihilism, the negation of medicine, to which the Vienna school was led. "Go to Vienna", people used to say in those days, "There everything is done for patients. They are diagnosed by Skoda and autopsied by Rokitansky."

A similar spirit pervaded German medicine in the Virchow era. Here also morbid anatomy and principally morbid histology dominated the clinical symptomatological-semiological picture of diseases. Virchow went even further and rejected the nosographical classifications of the British and French as "ontologies". That this principle too was wrong is shown by the chaos into which German medicine fell until its rescue by Frerichs, Leyden and others through introduction of the British and French nosology.

Morbid Anatomy and Histology as a branch of Pathology and thus of Physiopathology has its independence. The clinical scientist avails himself of the findings of this independent science but uses it to complete his disease pictures. This principle is being followed to-day.

(3). The introduction of the signs yielded by various laboratory methods marks a further step towards completion of the description of diseases. Urine, blood, vomit and fæces were examined macroscopically or by some rough methods by physicians of earlier ages, but it was only in the beginning of the nineteenth century that William Prout introduced more precise methods for various chemical examinations. In 1843 Gabriel Andral published his Essay on Hæmatology in which he studied the properties of the blood in various diseases.

Since then Pathology has given a great number of data on the biochemical, hæmatological and bacteriological aspects of disease in general. Clinical scientists avail themselves of these data to complete the description of each particular disease. The clinical scientist and the pathologist differ in their points of view. The pathologist uses biochemical, hæmatological and bacteriological data to study the general processes of disease. The clinical scientist uses the same data to complete his disease pictures. For him all these data are biochemical, hæmatological and bacteriological signs which he inserts in the frame of a particular disease picture, and thus all these pathological data are judged in the light of the general clinical picture.

The same can be said of the various functional tests. In 1866 Hutchinson investigated the functional capacity of the lungs with his spirometer. William Stokes, the Dublin clinician, described the "weakness or deficient muscular power of the heart" in 1856. Then, inspired by Claude Bernard and his stress on functional disturbances preceding anatomical lesions, the German school developed the study of functional tests. Adolf Kussmaul introduced gastric intubation in 1867, and with Leube he showed later the importance of this clinical method of exploration of gastric function. Similar functional tests were introduced for circulatory organs, for the liver and the kidneys. As usual, the technical developments made by the Germans were considerable, but the general idea underlying them was essentially wrong. With the exception of Kussmaul, who worked on British and French nosographical lines, most of them wanted to bypass nosology and to find tests presenting a physiological understanding of the individual patient. "We want to cure and not to classify", thundered Ottomar Rosenbach, the codifier of this line of research. However, the individual patient is not one or two tests but represents a totality of symptoms which can be understood only on the basis of previous knowledge of disease types, which represent totalities of symptoms. Thus these functional tests became useful only when connected with disease pictures, only when used to complete these pictures, and thus only when

Clinical Section

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[*February* 14, 1947]

Sclerodactylia with Œsophageal Lesion (3 Cases).—WILLIAM A. BOURNE, M.D., M.R.C.P.

Case I.—Mrs. A. B., aged 56. Raynaud-like symptoms from age 33. 1943: X-ray showed substernal thyroid with hiatus hernia. 1944: Burning of tongue on eating, with no obstruction. 1945: Blood-count—R.B.C. 4,480,000; Hb 68%; C.I. 0·68. 1946: Blood-count—R.B.C. 4,000,000; Hb 48%; C.I. 0·6.

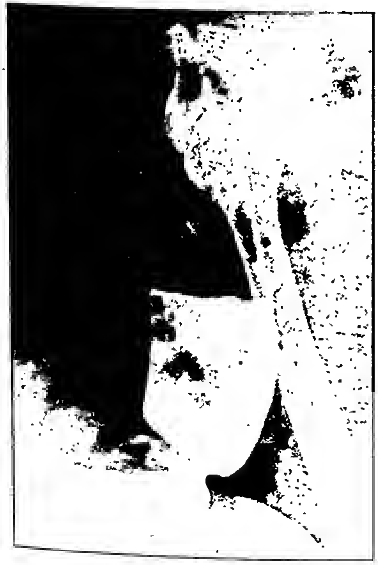


FIG. 1.—Case I. Œsophageal lesion associated with sclerodactylia. Atonic dilatation with hiatus hernia.

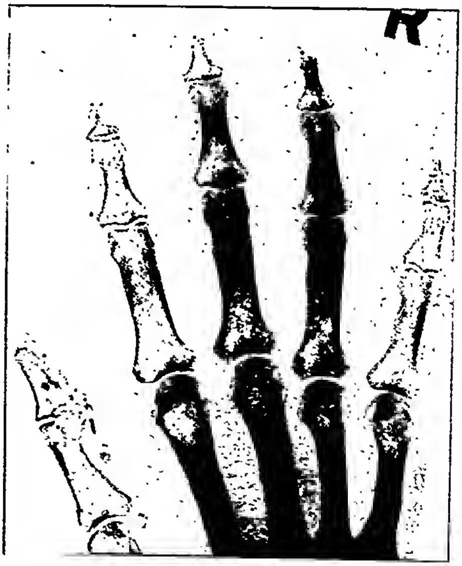


FIG. 2.—Case I. Sclerodactylia. Subcutaneous calcinosis with absorption of distal phalanges.

R.B.C. showed changes typical of severe hypochromic anæmia. Blood W.R. negative. Sputum negative for T.B. Stool negative for occult blood. Histamine test meal, achlorhydria. No flushing after 150 mg. nicotinic acid. X-rays showed dilated œsophagus with hiatal hernia (fig. 1). Lung fields showed slight basal fibrosis.

We take our remedies from any source, from old village women or from highly scientific laboratories. As Trousseau said, "La clinique prend son bien partout où elle le trouve". We can neither accept nor reject them on the basis of physiological and pathological considerations alone, but only on the basis of clinical observation. This principle should be applied to remedies whose physiological basis is debated, such as the homœopathic remedies, because their acceptance or rejection on the basis of *a priori* physiological thinking does not conform with our scientific method.

This chapter is based also on a special branch of Clinical Science, clinical pharmacology, which consists in study of the effects of remedies on healthy and diseased individuals. It is obvious that this branch is connected with pharmacology, mainly experimental, which is a branch of Pathology.

GENERAL CONCLUSIONS

There are three things in Medicine, the Art, Physio-pathology, and Clinical Science. These three are equally necessary but should not be confused, as is being done in most textbooks of History of Medicine.

The art of medicine consists in the application of scientific knowledge to the care of the sick. It demands special qualities of intuition and personality, but these qualities are useless without scientific knowledge. There has been a curious attempt in Germany—outside the universities—to build up a medicine without science, a medicine based only on intuition, personality, common sense and popular traditions. This movement originated with the physician of Bismarck, Ernst Schweninger (1850-1924), was adopted by the Nazis and was being developed in the Rudolf Hess Hospital of Dresden. Of course it failed. Medicine cannot be practised with "less science and more art" but needs "more science and more art".

Physio-pathology and Clinical Science are of equal importance. We cannot practise only on the basis of Physio-pathology, or even, as the Greek Empiricists and some early French nosologists of the Pinel type attempted to do, on the exclusive basis of Clinical Science.

Clinical Science is the natural history of diseases, a natural science comprising four chapters—the clinical descriptive, the pathogenic or physio-pathological, the ætiological and the therapeutic. The term should not be used in the restricted sense of clinical physio-pathology. It is a great and indispensable science, a branch of Biology.

Research physicians cultivate either Pathology or Clinical Science or both. They have, however, to keep their pathological and clinical scientific work in separate compartments.

The following quotation from an address by Sir James Paget in 1869 shows the real spirit of clinical science.

> "I am anxious to urge that all our work should be really clinical; all our chief studies among the living . . . I think there are even among ourselves signs of a want of faith in the power of clinical research; signs of too great readiness to reject results and suggestions which are not accordant with our belief in physiology or anatomical pathology; of too great readiness to accept and act upon deductions from any other sciences, though they are not approved by our own . . . We must believe and act on the belief that clinical science is as self-sufficient as any other. Self-sufficient indeed no science can be. All sciences are bound together by common facts and mutual illustrations and the same cardinal rules of study; yet each having its own subject-matter may claim a special range of knowledge, and within this range the highest right of judging what is true. This claim we must maintain for Clinical Science . . . I feel sure that Clinical Science has as good a claim to the rights and self-subsistence of science as any other department of biology; and that in it are the safest and best means of increasing the knowledge of diseases and their treatment."

Clinical Section

President—A. DICKSON WRIGHT, M.S., F.R.C.S.

[*February* 14, 1947]

Sclerodactylia with Œsophageal Lesion (3 Cases).—WILLIAM A. BOURNE, M.D., M.R.C.P.

Case I.—Mrs. A. B., aged 56. Raynaud-like symptoms from age 33. 1943: X-ray showed substernal thyroid with hiatus hernia. 1944: Burning of tongue on eating, with no obstruction. 1945: Blood-count—R.B.C. 4,480,000; Hb 68%; C.I. 0·68. 1946: Blood-count—R.B.C. 4,000,000; Hb 48%; C.I. 0·6.

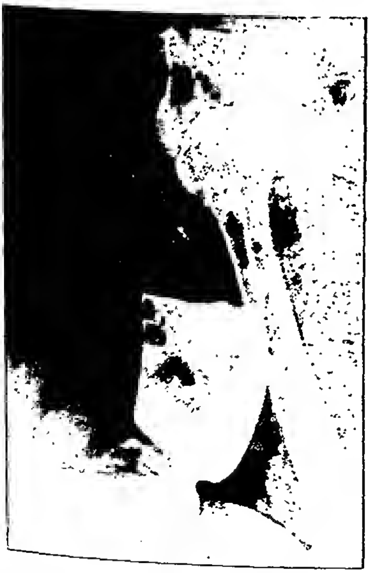


FIG. 1.—Case I. Œsophageal lesion associated with sclerodactylia. Atonic dilatation with hiatus hernia.

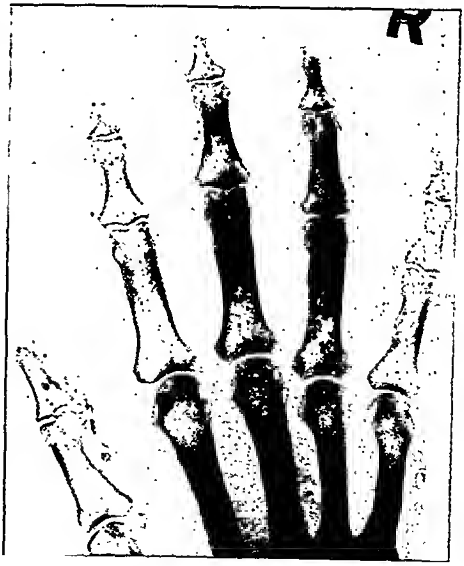


FIG. 2.—Case I. Sclerodactylia. Subcutaneous calcinosis with absorption of distal phalanges.

R.B.C. showed changes typical of severe hypochromic anæmia. Blood W.R. negative. Sputum negative for T.B. Stool negative for occult blood. Histamine test meal, achlorhydria. No flushing after 150 mg. nicotinic acid. X-rays showed dilated œsophagus with hiatal hernia (fig. 1). Lung fields showed slight basal fibrosis.

Hands showed calcinosis of subcutaneous tissues of digits with absorption of tips of terminal phalanges (fig. 2). Treatment with iron produced diarrhœa. Vitamin B complex relieved tongue symptoms. Transfusion raised Hb to 78% with relief of hand symptoms.

Case II (X-rays by courtesy of Professor J. McMichael).—Female, aged 60. Raynaud-like attacks since age 35. Dysphagia for thirteen years with repeated œsophageal dilatation. X-rays showed marked achalasia with traction deformity of upper œsophagus by fibroid changes in right lung apex, and shortening and absorption of distal ends of phalanges.

Case III (X-rays by courtesy of Professor Grey Turner and Professor McMichael). —Female, aged 56. Raynaud-like symptoms since age 54. Eighteen months' dysphagia and weight loss. Œsophageal dilatation gave only temporary relief. Following gastrostomy transferred to Hammersmith Hospital. X-ray showed obstructive lesion 2 in. above cardia with changes typical of new growth. Œsophagoplasty performed with relief of symptoms except for one bout of obstruction easily dilated. Histology of biopsied œsophageal wall: patchy hyperplasia and desquamation of the mucosa, œdema of the submucosa and infiltration with polymorphs, eosinophils, plasma cells and lymphocyte islets abutting on the muscularis suggesting lymphorrhages.

These three cases illustrate a relationship between sclerodactylia and œsophageal lesion recognized since 1903 (Ehrmann). From the Mayo Clinic Olsen, O'Leary and Kirklin report that 10% of cases of scleroderma seen between 1930 and 1943 had such a lesion, all the proved cases having sclerodactylia. English references are by Dowling, Lewis, and Prosser Thomas. The œsophageal involvement may simulate cardiospasm or carcinoma and may progress to marked atonic dilatation with hiatus hernia of short œsophagus type. Marked dilatation appears to produce few symptoms, but in cases showing less dilatation and more obstruction, Raynaud-like symptoms or frank sclerodactylia are important in diagnosis. (Two of the three cases reported were for a time regarded as carcinoma.) Case I presented several additional features. Hypochromic anæmia with glossitic symptoms suggested Plummer-Vinson syndrome, but X-ray findings were not characteristic. Length of history, absence of occult blood, and achlorhydria, rendered carcinoma, simple ulcer, or hæmorrhage from hiatus hernia unlikely. Bouts of severe diarrhœa were thought possibly due to sclerodermatous change in the small intestine, a suggestion supported by failure of nicotinic acid *per os* to produce cutaneous flushing. Notable improvement in hand condition followed elevation of hæmoglobin from 48% to 78% by transfusion. Wright and Duryee suggested the basis of symptoms in sclerodermia to be cutaneous ischæmia, and when appreciable anæmia is present transfusion should relieve ischæmic pain. The relation of thyroid disease to sclerodermia is doubtful (Banks, Bevans).

POSTSCRIPT (April 26, 1947).—The retrosternal goitre has since been successfully removed by Mr. Dickson Wright in spite of the rigidity of the head and neck.

REFERENCES

BANKS, B. M. (1941) *New Engl. J. Med.*, **225**, 433.
BEVANS, M. (1945) *Amer. J. Path.*, **21**, 25.
DOWLING, G. B. (1940) *Brit. J. Derm.*, **52**, 242.
EHRMANN, S. (1903) *Wien. med. Wschr.*, **53**, 1097, 1156.
LEWIS, T. (1940) *Brit. J. Derm.*, **52**, 233.
OLSEN, A. M., O'LEARY, P. A., and KIRKLIN, B. R. (1945) *Arch. intern. Med.*, **70**, 189.
THOMAS, E. W. PROSSER (1942) *Lancet* (ii), 389.
WRIGHT, I. S., and DURYEE, A. W. (1933) *Arch. intern. Med.*, **52**, 545.

Œsophageal Carcinoma Treated by Resection and Presternal Œsophago-Gastrostomy.—Hermon Taylor, F.R.C.S.

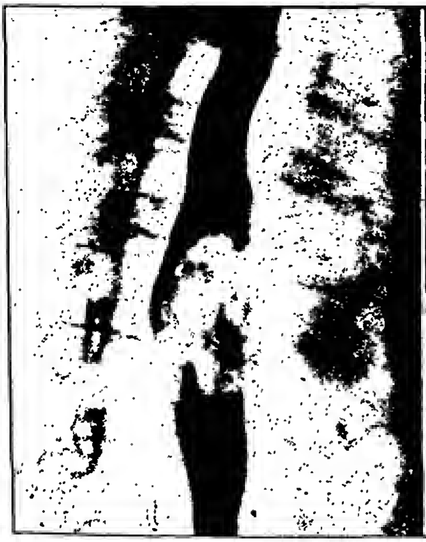


Fig. 1.—Mid-œsophageal growth before operation.

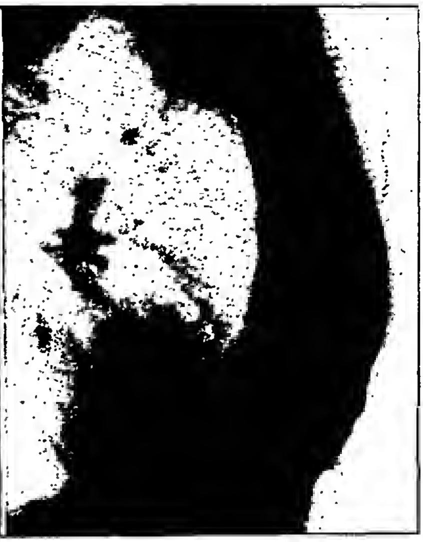


Fig. 2.—Lateral X-ray of presternal stomach with barium.

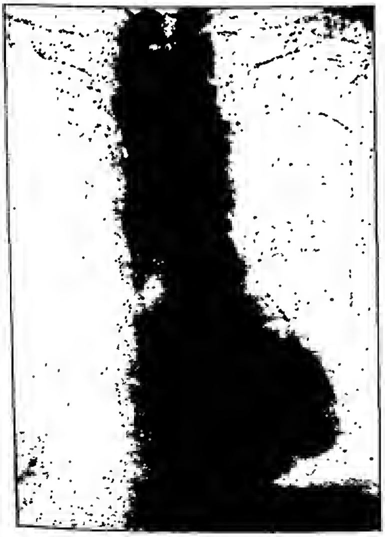


Fig. 3. —Antero-posterior X-ray of presternal stomach with barium.

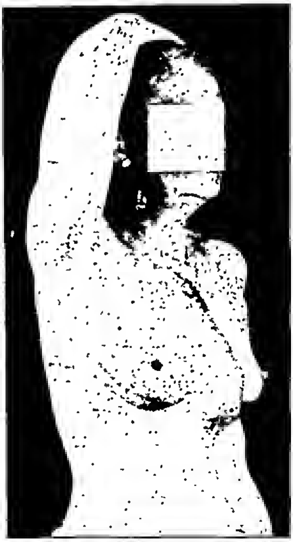


Fig. 4.–Patient 7 months after operation. Presternal stomach and the various incisions are well shown.

A. C., female, aged 53.

History of two months of dysphagia. X-ray showed cauliflower-like mass of growth in the œsophagus at the level of the sixth thoracic vertebra (fig. 1).

Stage I operation 11.7.46.—Right thoracotomy. Œsophagus mobilized. Growth 1½ in. long. Œsophagus was divided 1 in. above the growth so that the upper stump

Hands showed calcinosis of subcutaneous tissues of digits with absorption of tips of terminal phalanges (fig. 2). Treatment with iron produced diarrhœa. Vitamin B complex relieved tongue symptoms. Transfusion raised Hb to 78% with relief of hand symptoms.

Case II (X-rays by courtesy of Professor J. McMichael).—Female, aged 60. Raynaud-like attacks since age 35. Dysphagia for thirteen years with repeated œsophageal dilatation. X-rays showed marked achalasia with traction deformity of upper œsophagus by fibroid changes in right lung apex, and shortening and absorption of distal ends of phalanges.

Case III (X-rays by courtesy of Professor Grey Turner and Professor McMichael). —Female, aged 56. Raynaud-like symptoms since age 54. Eighteen months' dysphagia and weight loss. Œsophageal dilatation gave only temporary relief. Following gastrostomy transferred to Hammersmith Hospital. X-ray showed obstructive lesion 2 in. above cardia with changes typical of new growth. Œsophagoplasty performed with relief of symptoms except for one bout of obstruction easily dilated. Histology of biopsied œsophageal wall: patchy hyperplasia and desquamation of the mucosa, œdema of the submucosa and infiltration with polymorphs, eosinophils, plasma cells and lymphocyte islets abutting on the muscularis suggesting lymphorrhages.

These three cases illustrate a relationship between sclerodactylia and œsophageal lesion recognized since 1903 (Ehrmann). From the Mayo Clinic Olsen, O'Leary and Kirklin report that 10% of cases of scleroderma seen between 1930 and 1943 had such a lesion, all the proved cases having sclerodactylia. English references are by Dowling, Lewis, and Prosser Thomas. The œsophageal involvement may simulate cardiospasm or carcinoma and may progress to marked atonic dilatation with hiatus hernia of short œsophagus type. Marked dilatation appears to produce few symptoms, but in cases showing less dilatation and more obstruction, Raynaud-like symptoms or frank sclerodactylia are important in diagnosis. (Two of the three cases reported were for a time regarded as carcinoma.) Case I presented several additional features. Hypochromic anæmia with glossitic symptoms suggested Plummer-Vinson syndrome, but X-ray findings were not characteristic. Length of history, absence of occult blood, and achlorhydria, rendered carcinoma, simple ulcer, or hæmorrhage from hiatus hernia unlikely. Bouts of severe diarrhœa were thought possibly due to sclerodermatous change in the small intestine, a suggestion supported by failure of nicotinic acid *per os* to produce cutaneous flushing. Notable improvement in hand condition followed elevation of hæmoglobin from 48% to 78% by transfusion. Wright and Duryee suggested the basis of symptoms in sclerodermia to be cutaneous ischæmia, and when appreciable anæmia is present transfusion should relieve ischæmic pain. The relation of thyroid disease to sclerodermia is doubtful (Banks, Bevans).

POSTSCRIPT (April 26, 1947).—The retrosternal goitre has since been successfully removed by Mr. Dickson Wright in spite of the rigidity of the head and neck.

REFERENCES

BANKS, B. M. (1941) *New Engl. J. Med.*, 225, 433.
BEVANS, M. (1945) *Amer. J. Path.*, 21, 25.
DOWLING, G. B. (1940) *Brit. J. Derm.*, 52, 242.
EHRMANN, S. (1903) *Wien. med. Wschr.*, 53, 1097, 1156.
LEWIS, T. (1940) *Brit. J. Derm.*, 52, 233.
OLSEN, A. M., O'LEARY, P. A., and KIRKLIN, B. R. (1945) *Arch. intern. Med.*, 70, 189.
THOMAS, E. W. PROSSER (1942) *Lancet* (ii), 389.
WRIGHT, I. S., and DURYEE, A. W. (1933) *Arch. intern. Med.*, 52, 545.

Œsophageal Carcinoma Treated by Resection and Presternal Œsophago-Gastrostomy.—HERMON TAYLOR, F.R.C.S.

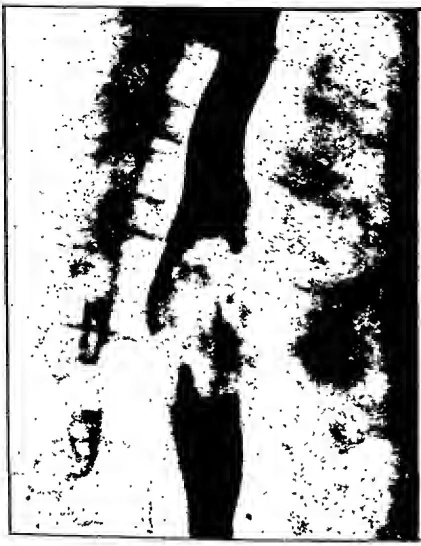


FIG. 1.—Mid-œsophageal growth before operation.

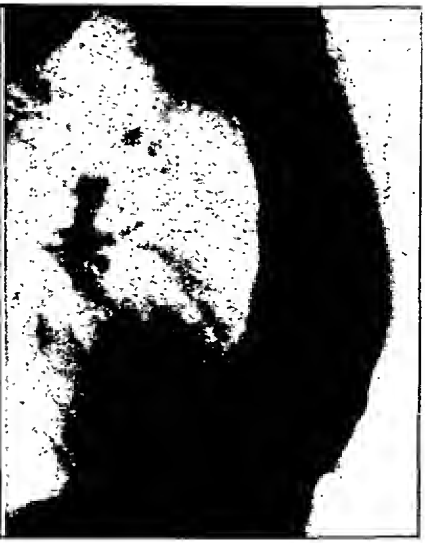


FIG. 2.—Lateral X-ray of presternal stomach with barium.

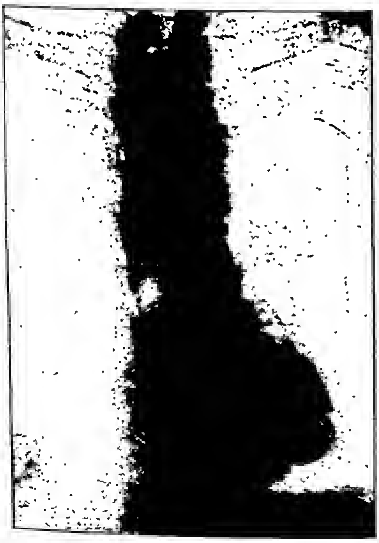


FIG. 3.—Antero-posterior X-ray of presternal stomach with barium.

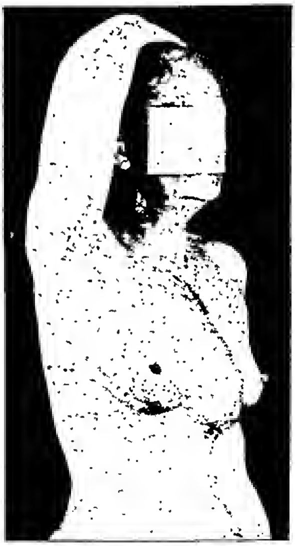


FIG. 4.–Patient 7 months after operation. Presternal stomach and the various incisions are well shown.

A. C., female, aged 53.

History of two months of dysphagia. X-ray showed cauliflower-like mass of growth in the œsophagus at the level of the sixth thoracic vertebra (fig. 1).

Stage I operation 11.7.46.—Right thoracotomy. Œsophagus mobilized. Growth $1\frac{1}{2}$ in. long. Œsophagus was divided 1 in. above the growth so that the upper stump just reached the suprasternal notch. Œsophagus was also divided below the growth and brought out into the epigastrium as an œsophagostomy, with an indwelling tube through the stomach into the duodenum, for feeding purposes.

Post-operative progress was uneventful with temporary exhibition of penicillin and aspiration of pleural fluid.

Stage II operation 8.8.46.—Stomach and lower œsophageal stump freed entirely from their proximal attachments. Lower œsophageal stump and upper half of the lesser curve together with lymphatic glands excised to complete the radical excision of area of possible extension of growth. Raw edge closed and infolded and the blind pear-shaped pouch of stomach, its stalk still attached as the pylorus with its vessels, now laid in a presternal subcutaneous position, the fundus reaching rather higher than the suprasternal notch where it lay under the upper œsophageal fistula.

No anastomosis was made at this stage.

The patient was fed by a tube through prepyloric gastrostomy via the pylorus to the duodenum. Post-operative progress was again uneventful.

Stage III minor operation 29.8.46.—Upper œsophageal stump was freed from the skin and anastomosed to the underlying pouch of stomach. Single layer anastomosis —no tension.

Post-operative progress was uneventful. The gastrostomy tube was withdrawn but the opening persisted.

Stage IV minor operation 6.10.46.—Closure of gastrostomy opening.

The patient is now able to eat an ordinary full meal. She is hungry for her food and is satisfied when she has eaten it. There has been no regurgitation into the mouth. She is conscious of the subcutaneous stomach which can be seen and palpated (fig. 4), but has no symptoms from its presence there. She lives a normal life and travels about the country in public transport at will.

Osteoporosis Circumscripta and Leontiasis Ossea Faciei Associated with Paget's Disease.—A. ELKELES, M.D.

A bus driver, A. J., aged 37, was transferred to the Manor House Hospital on 10.7.46, complaining of pain in his arms, shoulders, spine and knees.

History.—No previous serious illness. Six and a half years ago he noticed a swelling of his right cheek bone which gradually increased and was sometimes associated with severe neuralgic pain around his right eye.

Physical examination.—No abnormality except a diffuse hard swelling in region of his right upper jaw. Blood-count normal. W.R. negative.

Blood-chemistry.—Blood cholesterol 120 mg.; serum calcium 11·7 mg.; inorganic phosphorus 3·2 mg. per 100 c.c. Acid phosphatase 2·1 units; *alkaline phosphatase* 91 units (4 to 10 normal).

Radiological examination (24.7.46).—*Skull*: Enlargement and increased cloudy density of the right zygomatic bone in particular at the zygomatic arch. Thickening of the bony walls of the right maxillary antrum. Similar but less pronounced changes are visible on the left. Part of the maxillary antrum, the frontal sinus and the anterior ethmoidal cells on the right are obscured.

Large circumscribed rounded areas of osteoporosis are in the frontal and temporal regions near the base of the skull, through which the enlarged meningeal groove passes. These areas are surrounded by normal bone structures. Posterior half of the skull shows considerable osteoporosis interspersed with ill-defined nodular areas of bone condensation. Demarcation of this area from the anterior half of the skull is sharply defined but irregular in outline. There is marked thickening of the calvaria of the occipital and larger part of the parietal regions (two to three times that of normal thickness). Diploë can no longer be distinguished in the involved area and the lambdoid suture is obliterated (fig. 1). The remaining bones of the skeleton appear normal except the first lumbar vertebra, which shows early cotton-wool appearance, suggestive of Paget's disease. Diagnosis of osteitis deformans was confirmed by biopsy of the occipital portion of the skull by Professor Dorothy Russell.

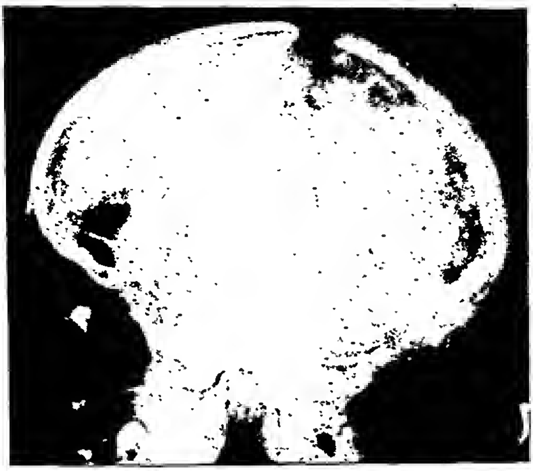


FIG. 1.

COMMENT

This case is an example of the difficulties which sometimes arise in the diagnosis and classification of bone diseases. The skull bones of this patient are the seat of apparently different pathological processes, and, unless the insidious forms in which Paget's disease may manifest itself in the skull bones are taken into consideration, the correct diagnosis may easily be missed. Osteoporosis circumscripta of the skull was first described by Schüller in 1926. But Sosman who re-examined one of Schüller's cases in 1927 established the relationship of osteoporosis circumscripta to Paget's disease for the first time, by examining trephined bone from the affected area. In his view osteoporosis circumscripta represents the absorptive-destructive phase of Paget's disease with the productive phase held in abeyance. Since then many reports have confirmed Sosman's observation and cases have been reported in which circumscribed osteoporosis of the skull was followed years later by typical Paget's disease.

The skull lesions in my patient represent different phases of Paget's disease simultaneously. The absorptive-destructive phase in its pure form is seen in the anterior half of the skull. The transition of the absorptive into the productive-repair stage with new but inferior bone formation is present in the posterior half, but has not yet the typical cotton-wool appearance of osteitis deformans. The new bone formation in this area points to marked osteoblastic activity, which finds confirmation in the much-raised alkaline phosphatase. The considerable thickening of the outer table and the diploë signifies typical Paget's disease. The findings provide strong evidence for the conception that osteoporosis circumscripta is a precursor of Paget's disease in the skull. The reason why circumscribed osteoporosis in osteitis deformans is met with solely in the skull bones may perhaps be explained by the pathological physiology of Paget's disease. According to Reifenstein and just reached the suprasternal notch. Œsophagus was also divided below the growth and brought out into the epigastrium as an œsophagostomy, with an indwelling tube through the stomach into the duodenum, for feeding purposes.

Post-operative progress was uneventful with temporary exhibition of penicillin and aspiration of pleural fluid.

Stage II operation 8.8.46.—Stomach and lower œsophageal stump freed entirely from their proximal attachments. Lower œsophageal stump and upper half of the lesser curve together with lymphatic glands excised to complete the radical excision of area of possible extension of growth. Raw edge closed and infolded and the blind pear-shaped pouch of stomach, its stalk still attached as the pylorus with its vessels, now laid in a presternal subcutaneous position, the fundus reaching rather higher than the suprasternal notch where it lay under the upper œsophageal fistula.

No anastomosis was made at this stage.

The patient was fed by a tube through prepyloric gastrostomy via the pylorus to the duodenum. Post-operative progress was again uneventful.

Stage III minor operation 29.8.46.—Upper œsophageal stump was freed from the skin and anastomosed to the underlying pouch of stomach. Single layer anastomosis —no tension.

Post-operative progress was uneventful. The gastrostomy tube was withdrawn but the opening persisted.

Stage IV minor operation 6.10.46.—Closure of gastrostomy opening.

The patient is now able to eat an ordinary full meal. She is hungry for her food and is satisfied when she has eaten it. There has been no regurgitation into the mouth. She is conscious of the subcutaneous stomach which can be seen and palpated (fig. 4), but has no symptoms from its presence there. She lives a normal life and travels about the country in public transport at will.

Osteoporosis Circumscripta and Leontiasis Ossea Faciei Associated with Paget's Disease.—A. ELKELES, M.D.

A bus driver, A. J., aged 37, was transferred to the Manor House Hospital on 10.7.46, complaining of pain in his arms, shoulders, spine and knees.

History.—No previous serious illness. Six and a half years ago he noticed a swelling of his right cheek bone which gradually increased and was sometimes associated with severe neuralgic pain around his right eye.

Physical examination.—No abnormality except a diffuse hard swelling in region of his right upper jaw. Blood-count normal. W.R. negative.

Blood-chemistry.—Blood cholesterol 120 mg.; serum calcium 11·7 mg.; inorganic phosphorus 3·2 mg. per 100 c.c. Acid phosphatase 2·1 units; *alkaline phosphatase* 91 units (4 to 10 normal).

Radiological examination (24.7.46).—*Skull*: Enlargement and increased cloudy density of the right zygomatic bone in particular at the zygomatic arch. Thickening of the bony walls of the right maxillary antrum. Similar but less pronounced changes are visible on the left. Part of the maxillary antrum, the frontal sinus and the anterior ethmoidal cells on the right are obscured.

Large circumscribed rounded areas of osteoporosis are in the frontal and temporal regions near the base of the skull, through which the enlarged meningeal groove passes. These areas are surrounded by normal bone structures. Posterior half of the skull shows considerable osteoporosis interspersed with ill-defined nodular areas of bone condensation. Demarcation of this area from the anterior half of the skull is sharply defined but irregular in outline. There is marked thickening of the calvaria of the occipital and larger part of the parietal regions (two to three times that of normal thickness). Diploë can no longer be distinguished in the involved area and the lambdoid suture is obliterated (fig. 1). The remaining bones of the skeleton appear normal except the first lumbar vertebra, which shows early cotton-wool appearance, suggestive of Paget's disease. Diagnosis of osteitis deformans was confirmed by biopsy of the occipital portion of the skull by Professor Dorothy Russell.

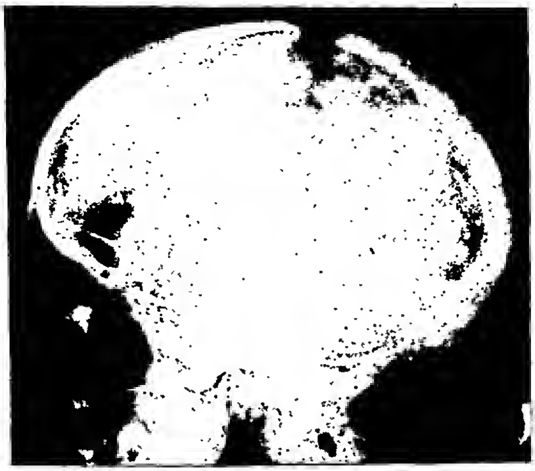


FIG. 1.

COMMENT

This case is an example of the difficulties which sometimes arise in the diagnosis and classification of bone diseases. The skull bones of this patient are the seat of apparently different pathological processes, and, unless the insidious forms in which Paget's disease may manifest itself in the skull bones are taken into consideration, the correct diagnosis may easily be missed. Osteoporosis circumscripta of the skull was first described by Schüller in 1926. But Sosman who re-examined one of Schüller's cases in 1927 established the relationship of osteoporosis circumscripta to Paget's disease for the first time, by examining trephined bone from the affected area. In his view osteoporosis circumscripta represents the absorptive-destructive phase of Paget's disease with the productive phase held in abeyance. Since then many reports have confirmed Sosman's observation and cases have been reported in which circumscribed osteoporosis of the skull was followed years later by typical Paget's disease.

The skull lesions in my patient represent different phases of Paget's disease simultaneously. The absorptive-destructive phase in its pure form is seen in the anterior half of the skull. The transition of the absorptive into the productive-repair stage with new but inferior bone formation is present in the posterior half, but has not yet the typical cotton-wool appearance of osteitis deformans. The new bone formation in this area points to marked osteoblastic activity, which finds confirmation in the much-raised alkaline phosphatase. The considerable thickening of the outer table and the diploë signifies typical Paget's disease. The findings provide strong evidence for the conception that osteoporosis circumscripta is a precursor of Paget's disease in the skull. The reason why circumscribed osteoporosis in osteitis deformans is met with solely in the skull bones may perhaps be explained by the pathological physiology of Paget's disease. According to Reifenstein and

Albright (1944) the initial lesion is a localized factor causing bone destruction. The affected bones are more susceptible to stresses and strains and as a compensatory mechanism increased osteoblastic activity sets in, laying down new matrix. It is therefore feasible that bones exposed to increased stresses, as spine, sacrum, pelvis and long bones, may fail to show the initial process of bone absorption, since the repair stage follows almost simultaneously. In the skull bones in which strain and stresses are minimal, bone repair may lag behind bone destruction.

The asymmetry of the patient's face, caused by a diffuse bony swelling of the zygoma and maxilla, calls for special comment. Kasabach and Gutman (1937) in their comprehensive paper on osteoporosis circumscripta of the skull and Paget's disease were able to collect 5 cases from the literature, to which they added 2 cases of their own with bony tumours of the maxillary region. In these cases it was invariably the upper jaw which showed the bony tumour and osteoporosis circumscripta was present in the adjacent frontal bone. The findings in my patient are almost identical with those described by Kasabach and Gutman. The bones of the face are only rarely involved in Paget's disease but, when affected, they produce the characteristic lion-like facies known as leontiasis ossea. It is doubtful whether leontiasis ossea represents a disease entity, since most of the reported cases are associated with Paget's disease and a smaller number with osteofibrosis generalisata Recklinghausen. The type Virchow, usually starting in childhood and hitherto considered an independent disease, may possibly be also part of a more or less generalized bone disease. This is suggested by recent reports of cases with Albright's disease (Pugh, 1945), in which involvement of the facial and skull bones showed the typical appearances of leontiasis ossea. The fact that in type Virchow the lesions are usually confined to facial and skull bones can perhaps be explained by their being the monostotic type of Albright's disease.

I should like to express my thanks to Lord Uvedale for kind permission to present the case and to Professor Dorothy Russell for the pathological report.

REFERENCES

KASABACH, H. H., and GUTMAN, A. H. (1937) *Amer. J. Roentgenol.*, **37**, 577.
PUGH, D. G. (1945) *Radiology*, **44**, 548.
REIFENSTEIN, E. C., and ALBRIGHT, F. (1944) *New Engl. J. Med.*, **231**, 343.
SCHÜLLER, A. (1926) *Brit. J. Radiol.*, **31**, 156.
SOSMAN, M. C. (1927) *Radiology*, **9**, 396.

[*March* 14, 1947]

Lymphadenoma.—LEO RAU, M.D.

This patient was shown to the Clinical Section May 1946 (*Proc. R. Soc. Med.*, **39**, 707). The post-mortem held on 17.1.47 confirmed the diagnosis. At autopsy, there was a large mass involving the left lower lobe of the lung, which penetrated the left diaphragm and pressed upon the left kidney, without involving it. There was a mass in the lower part of the right upper lobe, similar in appearance to that in the left side, but only 2 cm. in diameter.

Histology (Dr. George Lumb).—Lung masses show diffuse infiltration with small cells of reticulum cell type. There are frequent giant cells of Sternberg-Reed variety. It is clearly a reticulosis, and Hodgkin's disease seems the most likely variety. No evidence of carcinoma.

Hypothyroidism With Macular Abiotrophy and Inner Ear Deafness.—LEO RAU, M.D.

Male, aged 38, an artist. First seen in October 1939, complaining of deafness. This had started in 1937, and was getting worse. There was no tinnitus. The right ear was more affected than the left. In 1939, the clinical examination did not reveal any abnormality. The radiograph of the sinuses showed a fluid level in the right antrum. On aspiration, this fluid was clear and full of cholesterol crystals. He was seen again in January 1941, when his hearing was worse. In addition to this, he had noticed a central scotoma of the right eye since the summer of 1940, which was followed at Christmas by slight distortion of the central vision of that eye, and "whirling" in the centre of the right field.

On examination in January 1941 his face was puffy and he looked pale. His B.P. was 95/65. He was of normal intelligence, with an average memory, but showed signs of slow cerebration. In all decisions he was dependent on his wife. At times he was melancholic, and depressed, and complained of claustrophobia and lack of power of concentration. There were no headaches, convulsions or faints.

He was investigated as follows: Radiograph of skull normal. Audiogram, bilateral inner ear deafness (Mr. F. C. Ormerod). Left eye amblyopic; right eye central region of fundus resembles that seen in familial macular abiotrophy (Best's disease) of the type (presenile) associated with the name of Behr (Mr. Arthur D. Griffiths).

Blood Wassermann reaction negative.

Blood sugar tolerance—

Minutes:	fasting	30	60	90	130	240
Mg. %:	83	140	120	85	90	65

Water dilution and concentration good. Excretion slow and insufficient.

Basal metabolic rate −12%.

Family history.—His father died of heart disease, his mother is suffering from hypertension and diabetes. A male cousin of his father's has catarrhal deafness, and his niece is suffering from epilepsy. There is no consanguinity. He is practically a non-smoker, and does not drink any alcohol.

Treatment (20.3.41).—Thyroid by mouth 1 grain b.d. This was increased to 1 grain t.d. on 17.4.41, after the B.M.R. on 15.4.41 was − 1%.

Progress.—Marked general improvement from May 1941, the scotoma became less marked and his hearing improved. In March 1943, re-examination: hearing of left ear was practically normal, right ear considerably improved. At the same time Mr. Griffith reported that "the macular retinitis was absorbed, leaving him with perfect vision, a happy result, if a somewhat unusual one".

Re-examination in 1944 and in 1946, and again in March 1947, did not reveal any abnormality. He is still taking thyroid in small quantities, 1 grain per week.

Comment.—This combination of inner ear deafness and central blindness was unusual. The investigations as described above in detail were necessary to find out the cause. All the tests showed an abnormally low result, as is found in certain glandular disturbances, e.g. thyroid deficiency and anterior lobe deficiency. Normal sexual functions were against a pituitary disturbance. Further, the knowledge of the presence of cholesterol crystals in his antrum, and the presumed deposit of cholesterol in his retina seemed to point to a thyroid deficiency. Psychological abnormalities which this patient showed from 1926 to 1941 until the commencement of the thyroid treatment have not been stressed. They too form part of this syndrome.

Large Chronic Rodent Ulcer Treated by Radiotherapy.—J. A. C. FLEMING, F.R.C.S.Ed.

H. C., male, aged 68.

History.—Bayonet wound involving skin of lumbar region in First World War which healed.

1929: Ulcer above left eyebrow treated with radium.

1931: Excision of this area reported as rodent ulcer, subsequent to which he

Albright (1944) the initial lesion is a localized factor causing bone destruction. The affected bones are more susceptible to stresses and strains and as a compensatory mechanism increased osteoblastic activity sets in, laying down new matrix. It is therefore feasible that bones exposed to increased stresses, as spine, sacrum, pelvis and long bones, may fail to show the initial process of bone absorption, since the repair stage follows almost simultaneously. In the skull bones in which strain and stresses are minimal, bone repair may lag behind bone destruction.

The asymmetry of the patient's face, caused by a diffuse bony swelling of the zygoma and maxilla, calls for special comment. Kasabach and Gutman (1937) in their comprehensive paper on osteoporosis circumscripta of the skull and Paget's disease were able to collect 5 cases from the literature, to which they added 2 cases of their own with bony tumours of the maxillary region. In these cases it was invariably the upper jaw which showed the bony tumour and osteoporosis circumscripta was present in the adjacent frontal bone. The findings in my patient are almost identical with those described by Kasabach and Gutman. The bones of the face are only rarely involved in Paget's disease but, when affected, they produce the characteristic lion-like facies known as leontiasis ossea. It is doubtful whether leontiasis ossea represents a disease entity, since most of the reported cases are associated with Paget's disease and a smaller number with osteofibrosis generalisata Recklinghausen. The type Virchow, usually starting in childhood and hitherto considered an independent disease, may possibly be also part of a more or less generalized bone disease. This is suggested by recent reports of cases with Albright's disease (Pugh, 1945), in which involvement of the facial and skull bones showed the typical appearances of leontiasis ossea. The fact that in type Virchow the lesions are usually confined to facial and skull bones can perhaps be explained by their being the monostotic type of Albright's disease.

I should like to express my thanks to Lord Uvedale for kind permission to present the case and to Professor Dorothy Russell for the pathological report.

REFERENCES

KASABACH, H. H., and GUTMAN, A. H. (1937) *Amer. J. Roentgenol.*, **37**, 577.
PUGH, D. G. (1945) *Radiology*, **44**, 548.
REIFENSTEIN, E. C., and ALBRIGHT, F. (1944) *New Engl. J. Med.*, **231**, 343.
SCHÜLLER, A. (1926) *Brit. J. Radiol.*, **31**, 156.
SOSMAN, M. C. (1927) *Radiology*, **9**, 396.

[*March* 14, 1947]

Lymphadenoma.—LEO RAU, M.D.

This patient was shown to the Clinical Section May 1946 (*Proc. R. Soc. Med.*, **39**, 707). The post-mortem held on 17.1.47 confirmed the diagnosis. At autopsy, there was a large mass involving the left lower lobe of the lung, which penetrated the left diaphragm and pressed upon the left kidney, without involving it. There was a mass in the lower part of the right upper lobe, similar in appearance to that in the left side, but only 2 cm. in diameter.

Histology (Dr. George Lumb).—Lung masses show diffuse infiltration with small cells of reticulum cell type. There are frequent giant cells of Sternberg-Reed variety. It is clearly a reticulosis, and Hodgkin's disease seems the most likely variety. No evidence of carcinoma.

Hypothyroidism With Macular Abiotrophy and Inner Ear Deafness.—LEO RAU, M.D.

Male, aged 38, an artist. First seen in October 1939, complaining of deafness. This had started in 1937, and was getting worse. There was no tinnitus. The right ear was more affected than the left. In 1939, the clinical examination did not reveal any abnormality. The radiograph of the sinuses showed a fluid level in the right antrum. On aspiration, this fluid was clear and full of cholesterol crystals. He was seen again in January 1941, when his hearing was worse. In addition to this, he had noticed a central scotoma of the right eye since the summer of 1940, which was followed at Christmas by slight distortion of the central vision of that eye, and "whirling" in the centre of the right field.

On examination in January 1941 his face was puffy and he looked pale. His B.P. was 95/65. He was of normal intelligence, with an average memory, but showed signs of slow cerebration. In all decisions he was dependent on his wife. At times he was melancholic, and depressed, and complained of claustrophobia and lack of power of concentration. There were no headaches, convulsions or faints.

He was investigated as follows: Radiograph of skull normal. Audiogram, bilateral inner ear deafness (Mr. F. C. Ormerod). Left eye amblyopic; right eye central region of fundus resembles that seen in familial macular abiotrophy (Best's disease) of the type (presenile) associated with the name of Behr (Mr. Arthur D. Griffiths).

Blood Wassermann reaction negative.

Blood sugar tolerance—

Minutes:	fasting	30	60	90	130	240
Mg. %:	83	140	120	85	90	65

Water dilution and concentration good. Excretion slow and insufficient.

Basal metabolic rate − 12%.

Family history.—His father died of heart disease, his mother is suffering from hypertension and diabetes. A male cousin of his father's has catarrhal deafness, and his niece is suffering from epilepsy. There is no consanguinity. He is practically a non-smoker, and does not drink any alcohol.

Treatment (20.3.41).—Thyroid by mouth 1 grain b.d. This was increased to 1 grain t.d. on 17.4.41, after the B.M.R. on 15.4.41 was − 1%.

Progress.—Marked general improvement from May 1941, the scotoma became less marked and his hearing improved. In March 1943, re-examination: hearing of left ear was practically normal, right ear considerably improved. At the same time Mr. Griffith reported that "the macular retinitis was absorbed, leaving him with perfect vision, a happy result, if a somewhat unusual one".

Re-examination in 1944 and in 1946, and again in March 1947, did not reveal any abnormality. He is still taking thyroid in small quantities, 1 grain per week.

Comment.—This combination of inner ear deafness and central blindness was unusual. The investigations as described above in detail were necessary to find out the cause. All the tests showed an abnormally low result, as is found in certain glandular disturbances, e.g. thyroid deficiency and anterior lobe deficiency. Normal sexual functions were against a pituitary disturbance. Further, the knowledge of the presence of cholesterol crystals in his antrum, and the presumed deposit of cholesterol in his retina seemed to point to a thyroid deficiency. Psychological abnormalities which this patient showed from 1926 to 1941 until the commencement of the thyroid treatment have not been stressed. They too form part of this syndrome.

Large Chronic Rodent Ulcer Treated by Radiotherapy.—J. A. C. Fleming, F.R.C.S.Ed.

H. C., male, aged 68.

History.—Bayonet wound involving skin of lumbar region in First World War which healed.

1929: Ulcer above left eyebrow treated with radium.

1931: Excision of this area reported as rodent ulcer, subsequent to which he developed a soft subcutaneous swelling involving the underlying skin in this region.

1936: Wound in back began to ulcerate.

1937: Received treatment by radiotherapy to two lesions, believed to be rodent ulcers, involving the nose and forehead, did not draw attention to developing ulcer in lumbar region.

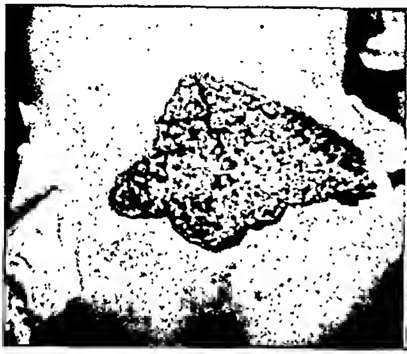


FIG. 1.—Before treatment, 24.6.45.

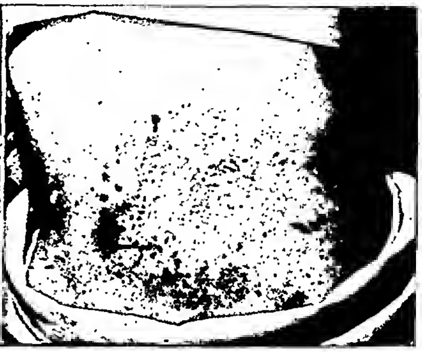


FIG. 2.—Six months after completion of treatment, 28.3.47.

24.6.46: Admitted to hospital with large ulcer involving skin of lumbar region measuring 11 cm. × 20 cm. No glandular involvement.

3.7.46: Biopsy from ulcer of back; report—basal-celled carcinoma with a tendency to squamous metaplasia.

15.7.46 to 23.9.46: X-ray therapy to back. 140 kV. Surface dose maximum. 5400 r (spaced) over 70 days.

Progress.—Involved area on back has healed slowly—has developed local recurrence at one corner [January 1947].

Arteriovenous Fistula Without a History of Trauma.—C. G. ROB, M.Ch., F.R.C.S.

Regular Sergeant R.A.F., aged 24. For six years he has noticed a vibration above his right clavicle. He has not taken any notice of this and has had good health up to the present time. Some ten years ago he had a blow on the back of the head but has had no other trauma to the neck and no penetrating wound.

He was admitted to hospital on 27.2.47 with a history of a sudden constriction in his chest at night which had been aggravated by deep breathing. He had "funny" feelings of the right leg and the whole of the right side with muscular spasms. The spasms lasted about half a minute. The pain in his chest persisted and spread to his throat where he had an aching feeling, and down the left arm on the inner side as far as the elbow. He was seen by a medical officer who heard a loud præcordial friction rub at the base and he was admitted as a case of pericarditis. An E.C.G. did not show changes suggestive of coronary thrombosis. His Wassermann was negative. His B.S.R. was 8 mm. in one hour (Westergren). His white count was 11,600, 81% polymorphs, falling in one week to 5,600, with 49% polymorphs. A throat swab grew hæmolytic streptococci.

He has a loud murmur occupying systole and diastole with a systolic accentuation below and above the right clavicle. This murmur is conducted up the line of the carotid vessels to the base of the skull, it is not conducted into the arm or below the third rib on the right side of the chest. There is a localized thrill above the right clavicle. His blood-pressure is equal in both arms 120/60. Occlusion of the fistula does not slow the pulse. No distended veins are visible, but a small soft pulsating mass is present at the site of the maximum murmur and thrill. An X-ray of chest shows no metallic foreign body, bony erosion or evidence of disease.

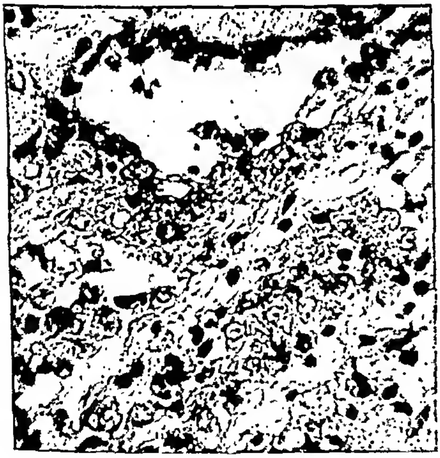
Diagnosis.—This is a small arteriovenous fistula probably on one of the branches of the thyreocervical artery. It is a single fistula, and therefore of an unusual type, for in the absence of a history of trauma it is probably congenital, whereas such arteriovenous fistulæ are usually multiple.

Malignant Lympho-endothelioma of Neck.—T. W. MIMPRISS, M.S.

Male, aged 46. Seen July 1946 with large, firm tumour right side of neck. Stated to have developed over two months.

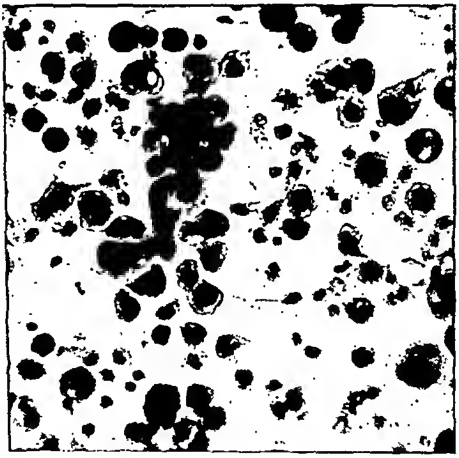
December 1946: Tumour in neck had grown considerably and there was a similar tumour in the right axilla. A pleural effusion on the right side and right recurrent laryngeal nerve paralysis had both occurred.

Following aspiration of pleural fluid the right upper lobe of lung was seen to be collapsed.



×300

FIG. 1.



×300

FIG. 2.

Section of the tumour shows malignant endothelioma; cells found in the pleural fluid are similar.

Diagnosis.—Malignant lympho-endothelioma of neck, infiltrating into axilla, pleura and mediastinum.

Treatment.—He is having a course of X-ray therapy.

Histological examination (Dr. J. Bamforth) shows that the tumour consists of spaces lined by large spheroidal cells showing a large pale vesicular nucleus and definite nucleolus. The spaces are separated by a loose stroma containing many cells of lymphocytic type. In addition, small aggregations of the large spheroidal cells are present in the stroma (fig. 1). Smears made from the pleural fluid, fixed in Schaudinn's fluid, showed large numbers of the large spneroidal cells found in the neoplasm (fig. 2). It is considered that this is a case of malignant lympho-endothelioma.

developed a soft subcutaneous swelling involving the underlying skin in this region.

1936: Wound in back began to ulcerate.

1937: Received treatment by radiotherapy to two lesions, believed to be rodent ulcers, involving the nose and forehead, did not draw attention to developing ulcer in lumbar region.

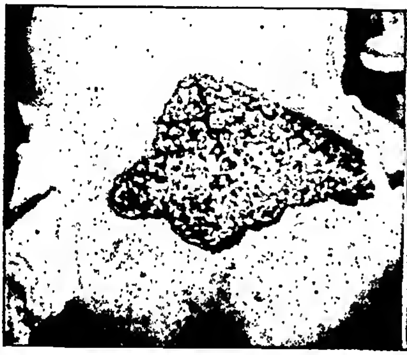


FIG. 1.—Before treatment, 24.6.45.

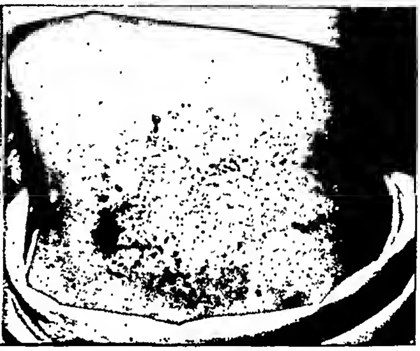


FIG. 2.—Six months after completion of treatment, 28.3.47.

24.6.46: Admitted to hospital with large ulcer involving skin of lumbar region measuring 11 cm. × 20 cm. No glandular involvement.

3.7.46: Biopsy from ulcer of back; report—basal-celled carcinoma with a tendency to squamous metaplasia.

15.7.46 to 23.9.46: X-ray therapy to back. 140 kV. Surface dose maximum. 5400 r (spaced) over 70 days.

Progress.—Involved area on back has healed slowly—has developed local recurrence at one corner [January 1947].

Arteriovenous Fistula Without a History of Trauma.—C. G. ROB, M.Ch., F.R.C.S.

Regular Sergeant R.A.F., aged 24. For six years he has noticed a vibration above his right clavicle. He has not taken any notice of this and has had good health up to the present time. Some ten years ago he had a blow on the back of the head but has had no other trauma to the neck and no penetrating wound.

He was admitted to hospital on 27.2.47 with a history of a sudden constriction in his chest at night which had been aggravated by deep breathing. He had "funny" feelings of the right leg and the whole of the right side with muscular spasms. The spasms lasted about half a minute. The pain in his chest persisted and spread to his throat where he had an aching feeling, and down the left arm on the inner side as far as the elbow. He was seen by a medical officer who heard a loud præcordial friction rub at the base and he was admitted as a case of pericarditis. An E.C.G. did not show changes suggestive of coronary thrombosis. His Wassermann was negative. His B.S.R. was 8 mm. in one hour (Westergren). His white count was 11,600, 81% polymorphs, falling in one week to 5,600, with 49% polymorphs. A throat swab grew hæmolytic streptococci.

He has a loud murmur occupying systole and diastole with a systolic accentuation below and above the right clavicle. This murmur is conducted up the line of the carotid vessels to the base of the skull, it is not conducted into the arm or below the third rib on the right side of the chest. There is a localized thrill above the

When seen again on 16.1.47, aged 21 months: Attacks had been controlled by diginutin, 4 drops daily. Satisfactory general development; no cyanosis; no clubbing; a systolic murmur over the whole heart, audible also over the aortic and pulmonary regions, the maximum in the 3rd left intercostal space near the left sternal border. The second sounds over the base were present. The exercise tolerance was good. Electrocardiogram: Wolff-Parkinson-White syndrome (fig. 2). A chest film showed the heart shadow to be enlarged and mainly globular in shape (fig. 3).

The first case of a short P-R interval with anomalous intraventricular conduction was published by Wilson in 1915 and a few isolated instances were reported subsequently. It was, however, not until Wolff, Parkinson and White published in 1930 a series of 11 cases that this syndrome was recognized as a clinical entity. A considerable number of explanations were put forward to account for this abnormality; they were listed in 1940 by Hunter, Papp and Parkinson. The hypothesis put forward independently by Holzmann and Scherf in 1932 and Wolferth and Wood in 1933 has now been accepted as affording the best explanation. According to this view the impulse originates normally in the sino-auricular node, but is conducted to the ventricles by an abnormal pathway, particularly the right lateral bundle, described by Kent in 1892 (often called the "bundle of Kent"). The assumption that the impulse is conducted through such an abnormal connexion as well as through the normal pathway via the atrioventricular node would account not only for the shortening of the P-R intervals and abnormal intraventricular conduction, but also for other features observed in this condition, viz. the abnormality in the Q-R-S complexes affects their first part either exclusively or predominantly whereas the appearance of the later parts of the Q-R-S complexes often is normal; moreover, if the features of the EC. revert to normal, either spontaneously or as a result of exercise or drugs, the interval between the beginning of the P waves and the end of the Q-R-S complexes (S-T junction) usually remains constant and is normal; lastly a high proportion of such cases have attacks of paroxysmal tachycardia, mostly of supraventricular origin.

The mechanism of the activation of the heart according to this view was well illustrated diagrammatically by Littmann and Tarnower (1946). Owing to the presence of an abnormal conducting bundle the normal impulse reaches abnormally quickly that part of a ventricle where the bundle terminates, since the physiological delay in the A-V node is absent; the result is a "pre-excitation" (Oehnell, 1944) of that particular part of one ventricle, which manifests itself in the EC. by an abnormally short P-R interval. From the area first activated the impulse spreads in the ventricles in an abnormal way, thereby giving rise to the abnormal shape of the first part of the Q-R-S complexes. Subsequently, however, as the normal conducting system is also functioning, the activation of the ventricles takes place in the normal way and it can thus be understood that the later parts of the Q-R-S complexes often have a normal appearance. This explanation also accounts for the transition of abnormal into normal forms and vice versa in the same patient and for the presence of transitional forms as well as for the fact that the P-ST junction interval remains the same with normal and abnormal complexes and is normal. The relative amounts of ventricular muscle activated through the abnormal connexion on the one hand and through the normal pathway on the other vary in different cases and in the same individual at different times. (Quite recently a case has been described by Kossmann and Goldberg (1947) in which the impulses seemed to have reached the ventricles exclusively by the abnormal connexion.) The frequent occurrence of attacks of paroxysmal tachycardia in such cases is accounted for by the presence of a circus movement, the impulse being conducted back to the auricles via the abnormal bundle.

This conception has been supported by more recent work in several ways. Glomset

[*May 9, 1947*]

Wolff-Parkinson-White Syndrome (Short P-R Intervals Associated With Disturbances of Intraventricular Conduction) With Attacks of Paroxysmal Tachycardia in an Infant Aged 8 Months Suffering From Probable Congenital Heart Disease.

—A. SCHOTT, M.D.

Cyanotic at birth; in an oxygen tent three days. Subsequently normal development until the age of 4½ months when frequent attacks of sickness and vomiting lasting from 24 to 36 hours started. Such attacks were heralded by a tachycardia of 220-260, starting and terminating suddenly.

On examination.—1.1.46, aged 8 months: Normally developed; no cyanosis; no clubbing. Electrocardiogram: Wolff-Parkinson-White syndrome (fig. 1). On screening the heart seemed to be enlarged and globular in shape.

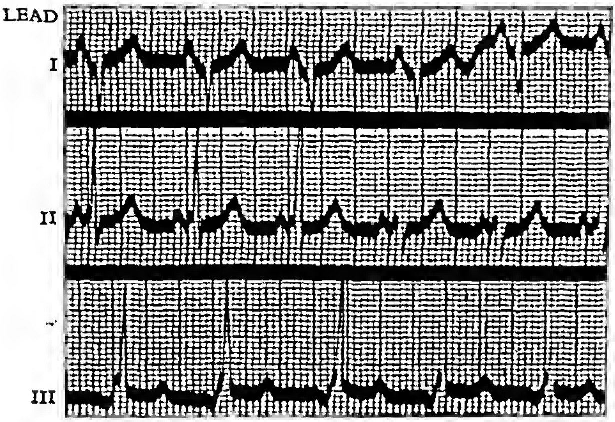


FIG. 1 (1.1.46).—Aged 8 months. Wolff-Parkinson-White syndrome. P-R intervals about 0·06 sec. (where measurable). Q-R-S complexes about 0·11 sec.

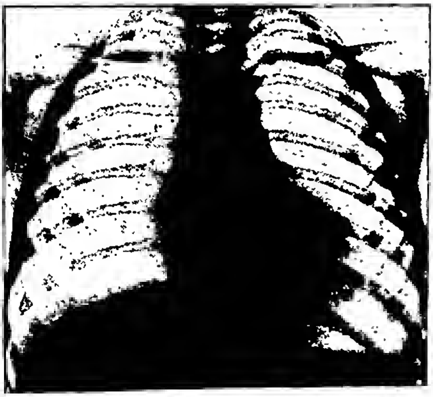


FIG. 3.

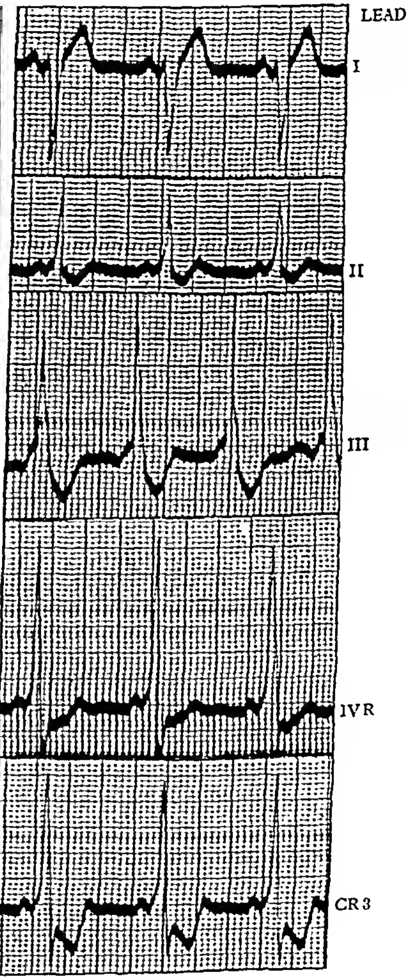


FIG. 2.

FIG. 2 (16.1.47).—Aged 21 months. Wolff-Parkinson-White syndrome. Note changes in the later portions of the Q-R-S complexes and in the T waves as compared with the previous record (*see also* text). P-R intervals about 0·08 sec. Q-R-S complexes about 0·12 sec. in the limb leads (where measurable), about 0·16 sec. in the chest leads.

FIG. 3 (16.1.47).—Aged 21 months. Chest film. Note enlarged heart shadow which is mainly globular in shape.

REFERENCES

BODLANDER, J. W. (1946) *Amer. Heart J.*, 31, 785.
BUTTERWORTH, J. S., and POINDEXTER, C. A. (1942) *Arch. intern. Med.*, 69, 437.
GLOMSET, D. J., and GLOMSET, A. T. A. (1940) *Amer. Heart J.*, 20, 389.
HOLZMANN, M., and SCHERF, D. (1932) *Z. klin. Med.*, 121, 404.
HUBBARD, J. P. (1941) *Amer. J. Dis. Child.*, 61, 687.
HUNTER, A., PAPP, C., and PARKINSON, J. (1940) *Brit. Heart J.*, 2, 107.
KOSSMANN, C. E., and GOLDBERG, H. H. (1947) *Amer. Heart J.*, 33, 308.
LITTMANN, D., and TARNOWER, H. (1946) *Amer. Heart J.*, 32, 100.
MOVITT, E. R. (1945) *Amer. Heart J.*, 29, 78.
NEUBAUER, C. (1945) *Brit. Heart J.*, 7, 107.
OEHNELL, R. F. (1944) *Acta med. scand.*, Suppl. 92.
ROSENBAUM, F. F., HECHT, H. H., WILSON, F. N., and JOHNSTON, F. D. (1945) *Amer. Heart J.*, 29, 281.
WILSON, F. N. (1915) *Arch. intern. Med.*, 16, 1008.
WOLFERTH, C. C., and WOOD, F. C. (1933) *Amer. Heart J.*, 8, 297.
WOLFF, L., PARKINSON, J., and WHITE, P. D. (1930) *Amer. Heart J.*, 5, 685.
WOOD, F. C., WOLFERTH, C. C., and GECKELER, G. D. (1943) *Amer. Heart J.*, 25, 454.

Dermatomyositis.—W. E. CLARKE, M.R.C.P. (for E. C. WARNER, F.R.C.P.).

M. E., female, unmarried, aged 43 years. Suffered from asthma for eighteen years prior to onset of present condition.

July 1945: Vivid erythema and burning sensation of skin of face, neck and front of chest to T.3; two months later swelling of left cheek spreading to involve whole face with weakness of facial muscles. January 1946: Marked general weakness and stiffness of whole body. November 1946: Erythema and irritation now both upper and lower limbs. Marked stiffness and general contracture of whole of musculature of body commenced and progressed. Slight dysphagia and dysarthria during past year not now present.

On admission (7.3.47).—Thinning of hair of scalp and eyebrows. Pigmented patches on scalp with some peeling of skin. Slight erythema of face. Patchy pigmentation of cheeks, neck and forearms and front of shins, also in axillæ. Muscles of face contracted and firm with œdema of subcutaneous tissue. Opening of mouth restricted; expressionless facies. Tongue protrudes poorly but palate and deglutition normal. Shoulder girdle, pelvic girdle and limb muscles all weak and sclerotic with some œdema of overlying tissue, most marked in distal parts of limbs.

Other systems normal: B.P. 130/78. Spleen not palpable.

Investigations.—Blood-count: R.B.C. 4,800,000; C.I. 1·0; Hb 96%; W.B.C. 7,000 (polys. 72%, lymphos. 21%, L. hyalines 4%, eosinos. 3%). Blood calcium 9·9 mg.%, B.S.R. 3 mm. in first hour, 9 mm. in second hour. Blood W.R. and Kahn negative. Blood phosphorus 3·1 mg.%. B.M.R. plus 15%. (Patient was rather apprehensive during tests.)

X-rays: Some osteoporosis of carpal bones, otherwise normal. No subcutaneous calcinosis. Lungs N.A.D. Teeth—two buried stumps in left lower molar region. Twenty-four hour creatine excretion estimations: 504, 460, 420 mg. daily.

Progress.—Rapid improvement while in hospital. Œdema much diminished in forearms and almost gone from face and legs. Muscles still extremely firm and contracted but now quite painless, even on stretching. Left lower molar roots removed under general anæsthesia with no flare-up in temperature. On culture grew a non-hæmolytic streptococcus.

Treatment so far has been symptomatic.

Comment.—The course of this case of dermatomyositis conforms to the usual description given of this condition. However, there was never any spontaneous pain, and at present even stretching the muscles causes no discomfort. The dysarthria and dysphagia were probably related to the weakness and stiffness of the tongue.

and Glomset (1940) not only confirmed Kent's findings of an abnormal connexion between auricle and ventricle, but found such connexions even more numerous than formerly assumed. Abnormal pathways were found histologically in one patient each, who had been known to have shown the W.P.W. syndrome, by Wood, Wolferth and Geckeler (1943), and by Oehnell (1944) respectively; in the former case, the connexion was found at the place where Kent had described it, in the latter it connected the left auricle with the left ventricle. The experimental work of Butterworth and Poindexter (1942) showed that the W.P.W. syndrome can be reproduced in dogs and cats by stimulating a ventricle with the normal auricular action current, amplified several thousand times; moreover, by reversing the direction of the current and stimulating the auricle by means of the amplified ventricular action currents, paroxysmal tachycardia could be produced. Lastly, Rosenbaum, Hecht, Wilson and Johnston (1945), by using unipolar leads from the œsophagus, præcordium and other parts of the thorax found that in cases showing the W.P.W. syndrome the dorsal wall of the ventricles is prematurely activated by impulses of supraventricular origin.

As late as 1946 it was stated that no cases had been reported in infancy (Littmann and Tarnower) although shortly before in the same year Bodlander published one case of this syndrome in an infant of 14 weeks; in view of the marked distortion of the tracing, however, caused by somatic tremor, it was not possible to make the diagnosis before the child was 2½ years old and the earlier tracing was misinterpreted; coarctation of the aorta also was present in Bodlander's patient. The present case seems to be the first one in which the diagnosis of this condition in an infant was made and the second one described of W.P.W. syndrome in infancy. The fact that congenital malformation of the heart also was present in both these cases may be of significance as congenital abnormalities of the heart often are multiple.

In regard to prognosis, this condition has generally been regarded as benign and any concomitant heart disease was usually considered to be coincidental. Some authors, however, have come to doubt whether this condition always is free from risk, and death in an attack of paroxysmal tachycardia has been reported (Oehnell). If the W.P.W. syndrome should be found to be a more frequent occurrence in infancy than hitherto assumed this would also have a bearing on the prognosis of paroxysmal tachycardia in infancy. It is usually stated that this arrhythmia is rare in infancy although according to Hubbard (1941) it is likely to be overlooked. If it is diagnosed the possible presence of a W.P.W. syndrome should be considered and in that event the prognosis would certainly be considerably better than when it is associated with severe infection, particularly diphtheria (Neubauer, 1945).

In the present case the prognosis will essentially depend on the associated structural malformation, the exact nature of which could not be diagnosed with any certainty at this patient's age. In trying to assess the marked changes in the EC. which have occurred between the ages of 8 and 21 months the fact has to be considered that the later tracing was obtained while the patient was having digitalis treatment; the marked alterations in the second part of the Q-R-S complexes and in the T waves need not necessarily be due to additional structural changes, but may, at least to a considerable extent, be an effect of the drug. It has been stated by Movitt (1945) that digitalis may not exert any influence on the aberrant bundle, whereas it would have the usual effect on the normal conduction path and this discrepancy would tend to aggravate the EC. signs of disturbances of intraventricular conduction.

Treatment by means of diginutin, 4 drops daily, was successful in preventing the attacks of paroxysmal tachycardia, but the dose had to be slightly increased when the patient was just over two years of age.

Section of Dermatology

President—SYDNEY THOMSON, M.D.

[*January* 16, 1947]

Lichen Planus in a Boy Aged 8 Years.—H. CORSI, F.R.C.S.

Duration two months. Eruption typical lichen planus.

There are no symptoms other than some itching after a bath.

Dr. H. W. Barber: Some years ago the children's nurse of a well-known surgeon consulted me for a severe and very widespread lichen planus. She asked me whether there was any risk of contagion to the infant she was tending. I replied that, although I believed the disease to be due to a virus infection, I had not met with an instance of apparent contagion. A few months later I saw the infant in question and it had quite typical lichen planus from which it made a spontaneous recovery. Considering the rarity of lichen planus in infants, I think this was probably a genuine example of contagion.

Hyperkeratotic Systematized Nævus with ? Bromide Eruption.—A. HARGREAVES, M.B. (for W. N. GOLDSMITH, M.D.).

Miss E. F., aged 52.

History.—At the age of 3 months, red patches were noticed on the skin, attributed at first to teething or vaccination. Generalized thickening and dark scaling of the skin were noted at about 1 year of age. The face, at first affected with the rest of the body, became clearer, while the legs got progressively worse and became painful; from time to time great lumps of skin separated from them. The pain was worse when she was lying than when sitting.

She attended school up to the age of 15, and apparently made average progress. Menstruation began at 16, and was normal until two or three years ago. Apart from self-administered aspirin, she had had no treatment, and washing had been minimal. On November 25, 1946, she was admitted to University College Hospital.

On admission.—The whole of her skin except the face and scalp was dry and rough. In many areas, especially the lower limbs and feet and hands, it was warty, the papilliform projections being in some parts acuminate and in others more rounded (mammillated). The palms and soles were greatly thickened, but smooth. On the upper limbs there was hypertrichosis (fig. 1). On the legs the papillomatous overgrowth reached an extreme degree, large fleshy red vegetations being covered by

The ætiology is still obscure. There was no preceding event or infection that could be associated with its onset. Her present progress is towards improvement, and any causative infective process seems to have subsided. There was no leucocytosis, the differential white cell count was normal, and the B.S.R. was not raised. There was no increase either in monocytes or in eosinophils, as has been described. There was no reaction to the removal of buried roots: these grew a non-hæmolytic streptococcus on culture. No consistent bacteriological findings have been described in the literature, and the muscle histology is not that of an acute infection. Griffiths and Dowling draw a close parallelism between the symptomatology, histology and biochemical findings in thyrotoxicosis and dermatomyositis. This case clinically is not thyrotoxic; her B.M.R. was raised, but she was apprehensive during repeated tests, and this presumably does not give a true indication of her B.M.R. Nor was there any undue sweating, which is often stressed as a finding. In this case too, the peripheral insulin test, used by Griffiths in these cases, was within normal limits. The blood calcium and phosphorus were normal, and there was no subcutaneous calcinosis or general osteoporosis. French writers have implicated the parathyroid glands, and claim good results after parathyroidectomy. The creatinuria is associated with the myopathy in these cases and in thyrotoxicosis, and cannot be used to relate them to a common ætiology.

Dr. F. Parkes Weber agreed that this was a remarkable example of subacute or chronic dermatomyositis (or "poikilodermatomyositis"), to be differentiated from mere symmetrical sclerodermia by the excess of the residual cutaneous pigmentation and the history of the striking facial erythema at the commencement. It was, however, now a case of "symptomatic scleroderma" (cf. F. P. Weber, "Rare Diseases," London, 2nd edition, 1947, p. 180) and should be treated by physical methods, such as massage, passive movements, "short waves," &c., with every chance of gradual, though slow, improvement, now that the most active and dangerous part of the disease was apparently over. He (Dr. Weber) did not think that the disease was of hormonal (endocrine) origin. He believed, however, that it represented an allergic manifestation towards some unknown kind of infection, the infection probably having little effect excepting in certain predisposed (hypersensitive or allergic) individuals. He stressed the analogy with the allergic theory of the manifestations of acute articular rheumatism.

patches. (2) The exuberant vegetating condition on her legs. (3) The pain in the legs. For the pain, which was intense and prevented sleep, analgesics and sedatives, including bromide, were given at first, but did not help. The three features above mentioned then aroused the suspicion of a drug eruption, especially bromide, superimposed on the nævus, and all sedatives were stopped.

Her blood bromide was found on December 5, 1946, to be 80 mg%, and a week later, 70 mg.%. This was calculated to be a much higher concentration than was likely to have been brought about by the amount we had given her. To help eliminate the bromide she was given sodium chloride by mouth.

Local measures consisted of Cyllin-M baths and varying strengths of salicylic acid ointment for the legs. Twelve days after starting the sodium chloride treatment, she became increasingly irrational, with visual and auditory hallucinations, and then drowsy. Ketones, but no sugar, were found in the urine. Treatment with sodium bicarbonate and glucose led to recovery of the ketosis, but she remained confused. Three weeks later Professor Himsworth advised a high-protein diet and big doses of vitamin-B complex. This was followed almost immediately by a striking improvement in her mentality.

The pain in her legs gradually got less from the time that sedatives were stopped and local treatment instituted. The offensive discharge steadily diminished and the warty masses were gradually reduced.

Inunction of an ointment containing potassium bromide 30% in soft paraffin on a relatively unaffected part of the skin caused no reaction.

Present condition.—The appearances have not changed except on the legs, where sepsis has been greatly reduced, and a good deal of the horny covering removed.

Comment.—The case is shown as an unusual systematized nævus of the ichthyosis hystrix group, and the question is raised whether the vegetating painful condition of her legs has been the result of prolonged bromide medication (of which there is no positive evidence), or whether it is just an exaggerated manifestation of the nævus. In either case, it is aggravated by sepsis and neglect.

Pityriasis Rubra Pilaris.—G. B. MITCHELL-HEGGS, O.B.E., F.R.C.P., and M. FEIWEL, M.B.

Miss J. F., aged 20.

At age of 12 sustained a compound fracture of the right arm. It was noticed that the scar when healed always remained red and had a tendency to scale. Two years later the skin below both eyebrows became red and scaly and showed no tendency to heal with local applications. The legs next became affected, showing a bluish-red discoloration followed by the appearance of horny rough papules, a condition which has persisted. Gradually other parts became affected, the arms, the upper part of the trunk and the face becoming red and scaly. The backs of the hands and fingers were involved four years ago but the changes are less obvious now. The scalp, the palms and the soles have always been clear. There has been little irritation throughout except during the past month, but there has been a feeling of tightness and constriction of the face, back and arms especially when the weather is cold. Desquamation has been severe at times. Local application of salicylic acid ointment and ung. aquosum, medication with vitamins, arsenic and thyroid, and calcium injections have merely reduced the amount of scaling. The patient has been receiving Grenz rays since September 1946 (Dr. Leitner).

Past history.—Measles, scarlet fever and chicken pox. Had urticaria and dermographism as a child.

thick masses of horny material mixed with debris and offensive pus (fig. 2). On the chest and upper limbs were some irregular flat red patches with sharp outlines.

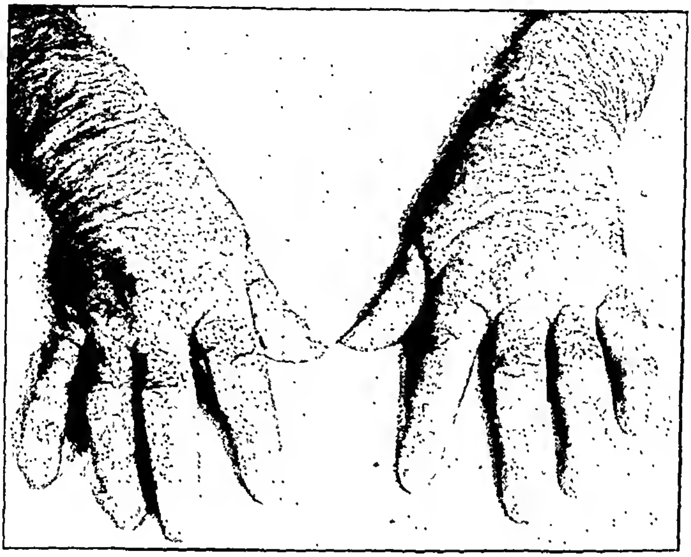


FIG. 1.

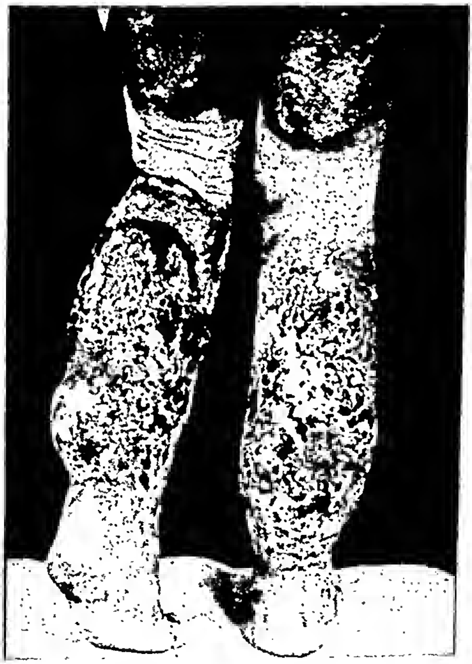


FIG. 2.
Condition on admission November 1946.

Course and treatment.—It was obvious that the essential trouble was a systematized warty and hairy nævus. Three unusual points attracted attention: (1) The flat red the right wrist and neck with very fine papules. The patches on the back, chest and thigh have a circumscribed but irregular and rather indefinite edge.

Blood examination.—Absolute count: R.B.C. 5,100,000; Hb (Sahli) 86%; C.I. 0·85; W.B.C. 5,900. Differential count: Polys. 61, lymphos. 28, monos. 5, eosinos. 4, basos. 2%.

Remarks.—Blood films show no anisocytosis, poikilocytosis or polychromasia. No nucleated red cells were seen.

Dr. W. Freudenthal: Dr. Mitchell-Heggs very kindly sent me the sections of his biopsies from back, chest and thigh for examination. They present the picture that one expects to find in poikilodermia vascularis, and in addition they all show a permeation of mesenchymal cells into the epidermis where they form small "cell nests". These cell nests are found in mycosis fungoides, and also in other reticuloses. The sections resemble those of Dr. Mitchell-Heggs's case of ? poikilodermia—? parapsoriasis—? premycosis, shown at the last B.A.D.S. meeting in which our French colleagues took great interest. The present case shows also clinically some resemblance to premycosis.

Pili Torti.—G. B. MITCHELL-HEGGS, O.B.E., F.R.C.P., and W. R. MAY, M.B., B.S.

Barbara, aged 4. Her mother states that she had very little hair at birth, and it never grew very much. She has had no serious illness, accidents or operations.

Family history.—No relatives are known to have had any unusual skin or scalp trouble.

On examination of the head the whole of the occipital area looks almost bald. Over the back and sides of the scalp the hair is now short and curly; it has never grown to a length of more than ½ in. in this region. The hair in the parietal and frontal area, where it is not subject to trauma, is between 2 and 3 in. long, but straight and brittle, and sticking out in an unruly fashion, as the hair will not stay in position after brushing. The hair has never required cutting. The eyebrows are also affected, but the eyelashes are normal. The nails and skin are normal. The child is healthy in all other respects. A brother aged 6 has normal hair.

On examination of the hair, there is apparent irregularity in the diameter of the hair. On microscopical examination, the irregularities are seen to be due to a twist of 180° at certain points; these points look like little nodes on direct examination, without lens. Histological examination of the hair follicles suggests that this twist in the hair is taking place in the follicles.

Dermatomyositis in a Child.—DOYNE BELL, D.M.

I first saw this child with Dr. Ungar in my Out-patients Dept. at the age of 2½ years. At the invitation of Dr. Wigley I now show him here, partly because I believe this to be an unusually early age at which to see so striking a case of dermatomyositis and partly in order to ask for suggestions as to treatment.

Male child, now aged 3 years. Birth-weight: 6 lb. 15 oz. Age of mother and father at birth—26. Breast fed for two months. Development normal. No previous illnesses. Vaccinated. Diphtheria immunization at usual times.

Well until one year ago, when lassitude and poor appetite were noted, red scaly areas of skin appeared on his nose and the back of the neck. Shortly afterwards red areas on the fingers and backs of his hands; these areas coalesced and the mother described them as looking like chilblains. These faded gradually when the area of skin began to stiffen. Stiffness spread to the forearms and to the elbows. Within two months stiffness developed in the feet and legs.

July 1946: Weight 1 st. 12 lb. 2 oz. Apyrexial during four weeks under observation in hospital, except for two peaks of temperature between 102° and 101° associated with a cold.

Family history.—No familial incidence of pityriasis rubra pilaris.

Present condition.—Face and neck have a uniform red discoloration. The upper part of the trunk, front and back, shows widespread red areas, with scaling more pronounced in some than in others. The breasts have a streaky dusky telangiectasia. The skin of the affected areas appears thickened. The "shoulder-strap" areas are curiously spared. The skin of the arms is almost uniformly covered with thickened, dusky red areas with some scaling. The dorsal surface of the proximal phalanges have very small indistinct discrete papules. The legs are covered with bright red areas and rough grating yellowish red papules centred round the follicles. The upper margin of the eruption is fairly sharply defined in the lower part of the thighs. Over each tendo Achillis and on the outer margin of the foot are rough, thick hyperkeratotic areas. The toes are red and smooth.

Biopsy from the skin at the back of the right arm: The epidermis varies in thickness due to varying depth of stratum granulosum. There is no hyperkeratosis but small areas of parakeratosis are present not related to the orifice of the sweat or sebaceous glands. Round-cell infiltration of superficial portion of the corium (Dr. Pike). Dr. W. Freudenthal confirmed the diagnosis of "Pityriasis Rubra Pilaris".

In the hope that vitamin-A therapy might help this case, estimations were carried out by Dr. Leitner and found to be normal.

	Blood carotene	*Vitamin A*
26.8.46	161 I.U.	113 I.U.
9.9.46	156 I.U.	103 I.U.

? Poikiloderma ? Premycosis.—G. B. MITCHELL-HEGGS, O.B.E., F.R.C.P.

Mrs. B. was referred to me on account of irritation on the back, chest and thighs for two months.

Past history.—Married, 3 children. All alive and well, no miscarriages.

Family history.—Father had gouty eczema, and one brother had alcoholic cirrhosis. No history of blood disease or of unusual skin condition.

Previous health.—In 1928 metrorrhagia and menorrhagia were treated by inducing an artificial menopause by treatment of the body of the uterus with radium (? 2250 mg. hr.) Mixed endocrine deficiencies following this procedure are likely to be a factor in the ætiology of this case.

History of present condition.—The patient, now aged 63, thinks she has had a rough patch on the lower part of her back, and on her chest and thighs since 1938, and that its appearance followed a type of sciatica which started with acute pain in the right calf followed by pain in the big toe and later in the other toes and ankle, ultimately causing dropped foot: this was supported by a garter-spring-toe-lift. The foot-drop is of uncertain origin and may have been due to a drug given for the sciatica.

The skin irritation commenced after a wasp sting in October 1946 and has gradually become more and more intense.

On examination.—General medical investigation showed no abnormality. The patient looks and feels quite well. Hair on the scalp is present, but there is no hair in the armpits. Her skin, generally, is unusually smooth. The surface of the skin on the back and chest shows a fine bran-like scaling with a diminution in thickness, atrophy in certain areas and infiltration in others.

On the deltoid region there is a rough red area; on both thighs, a reddish-brown area. The patch on the left thigh has a mottled appearance. There are areas of pallor with a network of vascularity. An erythematous patch is also present on

In recent times there have been rather more ulcers which have appeared higher on the legs around the knees.

The lesions are purplish nodules, palpably deep in the subcutis, and some of them break down into indolent ulcers. Healed lesions show marked scarring. There is no apparent disease of the veins.

There was no apparent response to treatment with calciferol over three months.

The lesions here resemble those of erythema induratum, but there is no evidence of tuberculosis, and the disease has been present for twenty years.

Dr. C. H. Whittle: I was wondering if this could possibly be a case of epidermolysis bullosa. That may seem a somewhat fantastic suggestion but I saw a case a month ago presenting chronic ulceration for many years of the legs and also of the back in a man about whom we were very puzzled. I took him into hospital for investigation and found he had been in several years ago, and I had then with confidence and without difficulty diagnosed epidermolysis bullosa. Under observation for a few weeks he produced typical bullæ on prominent parts. The histology might settle the question in this case.

Dr. J. E. M. Wigley: Would the President say whether he thinks this case would come into the category described by Dr. Arthur Whitfield as erythema induratum—not of tubercular origin?

The President: It is true that in most of Whitfield's cases the lesions were in the thighs and did not break down. He was convinced that they were the result of septic foci elsewhere; and it is also true that the number of his cases which I saw at that time did clear up. Unfortunately, I did not see the particular case Dr. Wigley has in mind.

Dr. C. H. Whittle: Were not Whitfield's cases occurring in middle-aged women? The patient Dr. Wells refers to is about thirty years of age.

Dr. G. C. Wells: I believe the cases Whitfield described occurred in women of about forty years of age, in which the lesions were more painful and in which no tuberculous ætiology was found. At about the same time Galloway described the histology in which he emphasized the sclerosis in small vessels and fat necrosis, but again none of the cases was tuberculous and I gather that he got no closer to the true ætiology.

I should question an epidermolysis bullosa. The lesions in this case are too deep and they appear as nodules which in many instances do not break down. The lesions around the knees have broken down. They were explored for micro-aerophilic streptococci, but no organisms grew either aerobically or anaerobically.

Leukæmia Cutis ? Myeloid Leukæmia.—E. Colin Jones, M.B.

Mrs. K. P., aged 47. Was referred to me on December 30, 1946, giving the history that she had developed a sore throat two to three weeks ago, followed two weeks later by the widespread rash now evident.

Careful questioning at a later date revealed that she had had swelling of her ankles off and on for one year, and been markedly dyspnœic.

Previous history.—Hysterectomy eighteen months ago (bleeding fibroids). No blood examination.

On examination.—An ill-looking woman. Fever and tonsillar remnants, with ulceration and necrosis, left more than right. Recent bleeding from the gums, but for the most part not affecting the buccal mucosa. Generalized glandular enlargement, most marked in the cervical triangles, and less so in the axillary and inguinal regions. Spleen and liver easily palpable, two f.b. Œdema of legs, no obvious cause.

She has a widespread nodular and infiltrated eruption, most marked on the abdomen (when originally seen limited to this area, but now affecting the trunk and limbs). The lesions on the breasts are petechial, hæmorrhagic, and indurated, but for the main part tumour-like infiltrated nodules covered by normal skin.

Investigations.—Wassermann negative. R.B.C. 2,900,000/c.mm.; Hb 56% Haldane; C.I. 0·9; W.B.C. 56,000/c.mm. Differential: Myelos. 88, premyelos. 2, At this time there were scaling red areas on nose and on the right side of the back of the neck. The whole of the extensor aspect of the forearms and legs was pigmented as if sunburned.

The movements of the wrists were restricted, and also of the ankles, and the skin covering the fingers was atrophied and inelastic.

Investigations (July 1946).—Tuberculin jelly test negative; blood-count within normal limits; urine normal; E.S.R. (Westergren) 6 mm. in 1 hr. to 16 mm. in 2 hr.; X-rays of limbs, chest and skull normal (Dr. F. Tierney).

Chemical investigations (Dr. J. Paterson).—Blood urea 22%, blood uric acid 4·2, blood cholesterol 210, serum sodium 375, serum potassium 20, plasma chloride 270 mg.%. Daily urinary excretions total: Nitrogen 5·89 grammes; creatine 157 mg.; creatinine 327 mg.

Insulin resistance test (*see* Griffiths, *Brit. J. Derm.*, 1940, **52**, p. 295). Using 2·5 units of soluble insulin intravenously and 25 grammes of glucose p.o. results are: *Capillary*: Fasting 107, 30 minutes 130, 60 minutes 146. *Venous*: Fasting 77, 30 minutes 99, 60 minutes 125.

There has been a gradual progression during the past few months. He now shows scleroderma of the hands and feet with myositis of the legs and forearms and areas of de-pigmentation of these areas and also of the back of the neck.

There are small discrete glands in the back of the neck, left axilla and groins. No splenomegaly.

Dr. H. Corsi: I think benefit might result to the child from treatment with short-wave therapy; I suggest that one limb be so treated and the effect observed.

Dr. G. B. Mitchell-Heggs: I suggest a sympathectomy as a trial on one side, because the adults we see with similar conditions are often relieved by sympathectomy.

Dr. J. E. M. Wigley: I think any question of sympathectomy should be approached with extreme caution.

The President: Recently I had occasion to see a middle-aged sea captain with what was, apparently, an acute scleroderma of the chest. From the clinical point of view I had no doubt about that. The disease progressed rapidly and became much more obviously a dermatomyositis. The patient died within two or three months. The histological picture of the skin and of the subcutaneous tissues was that of scleroderma, while that of the muscles showed a sclerodermatous infiltration plus large amounts of what were undoubtedly typical myositic degeneration, &c. That was the most striking case of the type that I have seen. I confess that I have been dubious, formerly, as to the connexion between the two diseases.

There is one feature about this particular child which undoubtedly suggests dermatomyositis; the classical mode of onset is so well described. From the purely clinical point of view to-day one would have to think of the third group of scleroderma in which changes start in the deeper tissues and spread towards the surface and into the muscles. In this particular case it seems wise to have a biopsy to see if there are any pathognomonic changes in the muscle.

Recurrent Ulcers of the Legs.—G. C. WELLS, M.R.C.P.

Miss B., aged 35. School teacher.

This patient first noticed lumps about the ankles at the age of 14 years. Some of the lesions went on to ulcerate, and she has had trouble with these indurated lesions and ulcers over the last twenty years. At times she has been free of trouble for as long as six months, and the lesions tend to clear with rest or while she is on holiday.

The lesions do not appear to vary with the seasons, although she has the tendency to acrocyanosis and coldness of the extremities which usually accompanies Bazin's disease.

General health has been good, apart from migrainous headache. There has never been anything to suggest tuberculosis, and X-ray of the chest is negative.

Section of Orthopædics

President—V. H. ELLIS, F.R.C.S.

[*December* 3, 1946]

Diaphyseal Aclasis.—G. O. TIPPETT, F.R.C.S.

Man, aged 32. Neuritis of the left arm together with an increasing swelling below the outer end of the left clavicle which he had noted for three months. No history of injury. An X-ray showed an osteoma growing from the outer end of the left clavicle which was no doubt pressing upon the inner part of the brachial plexus (see fig. 1). Further X-rays showed osteomata growing from the scapulæ and the lower ends of both femora.

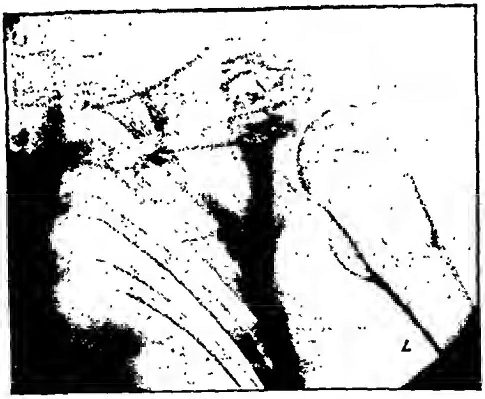


FIG. 1.—Case of diaphyseal aclasis. Osteoma of clavicle.

Cyst in the Femur.—G. O. TIPPETT, F.R.C.S.

Child, aged 8, was knocked over by a dog in January 1945. Admitted to hospital suffering from a fracture through the outer end of the neck of left femur. An X-ray showed that the fracture had taken place through a solitary cyst in the outer end of neck and upper part of shaft of femur. The fracture was immobilized in a plaster spica for three months at the end of which time the cyst appeared to have grown larger. During the next eight months the child was allowed to walk on a weight-relieving caliper. During this time the X-ray taken shows that the appearance of the cyst is greatly enlarged with much periostitis.

neutrophil myelos. 2, neutrophil metamyelos. 1, neutrophil polys. 3, lymphos. 0·5, promonos. 2·5, monos. 1%.

Dr. M. O. Skelton reports appearance is that of a myeloid leukæmia in a myeloblastic phase—i.e. with many circulating blast cells.

It may be an acute myeloid leukæmia *ab initio*, or an acute phase in a chronic leukæmia.

Biopsy.—There is a zone of large mononuclear cells lying beneath the epidermis. This zone of infiltrating cells lies in the most superficial part of the cutis, for the most part, with some tendency to show deeper aggregations in small areas. These cells appear to be of the same type as the blast cells in the circulating blood, and the condition to be a leukæmic infiltration of the skin.

Dr. W. A. Bourne saw this case three days ago, and considered it was probably a monocytic leukæmia, passing into a myeloid leukæmia (Naegeli type). The only points against it are the prominent spleen and absence of lesions in the buccal mucosa.

Lupus Vulgaris with Epithelioma and Mutilations.—G. B. MITCHELL-HEGGS, O.B.E., F.R.C.P., and J. R. OWEN, M.R.C.P.

Housewife, married, aged 52. History of red scaly patches developing on the face at the age of 24. Subsequent appearance of similar lesions on body and hands, which later spread to the arms. Attended for treatment at the Royal Berkshire Hospital, Reading, when lesions had already been present for over a year. No notes of early treatment available, but X-rays said to have been used in several areas. After receiving this, and other forms of treatment over a period of several years, she ceased attending, but returned again in August 1946, on one occasion only.

There is no history of any other illness save laryngitis a few weeks before the onset of the skin condition, and this was not considered at the time to be tuberculous, although it took some months to clear up, nor is there any record of tuberculous disease, or disease of the skin, amongst relatives.

The case presents very numerous patches of typical lupus vulgaris over the face, trunk, and upper limbs. The hands are grossly affected, with scarring, atrophy, swelling, necrosis, loss of phalanges, and ulceration. The face is extensively infiltrated with lupus in its later stages, and the left maxillary region presents an enormous, deep, foul-smelling ulcer which has eroded the antrum and nares.

It has been impossible to investigate or treat, owing to the patient's failure to attend. Her very good reasons for not attending were that no treatment had ever helped her, and that she was unable to bear the remarks made by her fellow out-patients in her hearing.

Dr. Whittle: How are the mutilations which produce the curious horny changes on the tips of the fingers explained?

Dr. Owen: I think endarteritis due to the tuberculous process may have caused the changes at the finger-tips.

monthly intervals according to the amelioration of symptoms and tendency to relapse. After six doses the patient is instructed to return for an injection when required.

The joint can be injected from the side, from the back, or from the front. Of these the anterior approach seems to be the easiest, the least painful and also the more certain. The surface marking which was drawn on the thigh of the case shown is simple in the extreme. The femoral artery is marked on a line joining the symphysis pubis with the upper edge of the great trochanter. The needle is inserted vertically on this line an inch or so outside the artery. A local anæsthetic is not really necessary but the use of a fine procaine needle as a probe to test the thickness of the capsule of the joint, and whether the point meets with bone, cartilage or tender synovial membrane, is a help.

When bone is encountered the injection can still be given provided that the needle has a sufficiently short bevel to drive the solution in between the closely apposed layers of the synovial membrane.

In a small proportion of cases, fluid is present in the joint so that it is as well to try aspirating with an empty syringe before attaching the syringe containing the solution.

Grant Waugh advises infiltrating the tissues in the neighbourhood of the joint. I do not do this intentionally, though the effect seems to be quite satisfactory as long as the point of the needle is inside the capsule. No surgical accidents have occurred.

We have now carried out many hundreds of these intra-articular injections of the hip-joint at the Clinic and I can therefore speak with some confidence of their value. I cannot claim that these alone will arrest the progress of osteo-arthritis of the hip-joint, because all cases are given vaccine therapy as a routine. In addition, special exercises are given for stretching the adductors of the thigh, counteracting flexion and eversion deformities and strengthening atrophied muscles.

Over the last twenty-five years comparative skiagrams have demonstrated arrest of the disease process in a high proportion of cases, but since the introduction of acid phosphate injections, some joints seem positively to have improved as in the case of the patient shown to the meeting.

[Lantern slides were put on the screen, and skiagrams shown of a joint injected with a contrast medium.]

Osteoid-Osteoma of Upper End of Ulna.—D. WAINWRIGHT, F.R.C.S.Ed.

Early in February 1944, Jessie E., an unmarried girl of 18, employed in a pottery, was referred with a history of pain and increasing stiffness of the left elbow, which she first noticed fourteen months previously. She had been treated as a case of monarticular arthritis, with myocrysin, following an X-ray examination in April 1943 which did not show any bone abnormality.

She was complaining of intermittent pain in the left elbow-joint, which had been gradually getting worse and which troubled her at night and was aggravated by use of the joint. There was no history of injury.

Examination revealed an appreciable thickening of the upper end of the ulna with some tenderness on deep pressure; no local redness or heat. Movements of the elbow-joint were limited to about 45 degrees of extension and 30 degrees of flexion. W.R. was negative. B.S.R. 4 mm. in first hour. Blood-count normal.

X-rays: Considerable thickening and sclerosis of the upper end of the ulna with a well-defined lesion involving the articular surface, showing considerable mottled calcification and surrounded by a faint translucent line of demarcation.

The possibility of this being an example of an osteoid-osteoma was considered, but the tumour—if such it was—appeared to be very inaccessible, and she was

The case was shown for confirmation as to the nature of the condition though it is probable that the condition remains one of simple cystic disease. The appearances might also suggest that the condition was a myeloma. At the meeting it was pointed out that the age of patient was against the diagnosis of myeloma and in favour of a loculated cystic condition.

The treatment advised by several members was exploration of the area with, probably, scraping out the abnormal tissue and packing the cavity with bone chips.

Typhoid Osteitis of the Long Bones.—E. T. BAILEY, F.R.C.S.

A. S., merchant seaman, aged 20. 31.10.45: While serving in Hospital Carrier running between Southampton and Ostend he contracted severe typhoid fever with positive Widal reaction and positive culture typhoid bacilli in the blood and fæces. Gradual recovery followed, but, whilst still convalescing five months later, he developed nodes on both tibiæ, right fibula and left radius and ulna. These caused general bone aching and local tenderness. He was treated conservatively for the first three months by physiotherapy and local applications without improvement, until definite subperiosteal abscesses formed, for which local aspiration with penicillin replacement was carried out and combined with systemic penicillin. Culture of aspirated pus was sterile, but the condition progressed.

25.6.46: The affected areas of the left tibia and left radius were excised and the area of the right fibula curetted. Operation findings showed small, clean-cut cavities containing gelatinous material enclosed in dense sclerotic bone. Following the operation, subsequent progress was uneventful apart from some delayed skin healing at site of previous abscess formation. Bone symptoms were completely relieved.

Histological report of bone and adjacent tissue excised at operation: Chronic purulent inflammation including some large cells of "typhoid" type in fragments of fibrous tissue with a few trabeculæ of new bone formation in two specimens.

All blood tests, including blood-count, W.R., Kahn, G.F.T. and agglutination tests were normal. B.S.R.: Fall in one hour 5 mm. The characteristic features of the case were the selection of the cortex for the site of bone infection, the chronicity with bone sclerosis and failure to respond to conservative measures.

Osteo-arthritis of the Hip-joint treated by Intra-articular Injections.—H. WARREN CROWE, D.M.

Male, aged 56. Began to feel pain in 1940. No trauma. No family history of arthritis.

This case is a good example of the effect of intra-articular injection of the hip-joint.

A few months ago at a meeting of the Section on the surgery of the hip-joint, Grant Waugh described his results in some twenty-five cases. I should like here to pay my tribute to his originality and to express my thanks to him for having been the initiator of such an exceedingly helpful method of treatment. Grant Waugh uses a solution of procaine and lactic acid. At the Charterhouse Rheumatism Clinic we have substituted for this two preparations of acid-buffered salts: acid potassium phosphate (A.P.P.) and acid magnesium phosphate (A.M.P.). Whether procaine is added or not the effect is the same but it does delay reaction so that out-patients can get home in comfort. A.P.P. is less drastic, can be given in larger amounts, being much less liable to provoke reaction, but its effect is less prolonged. The first dose is 20 c.c. of A.P.P. followed a fortnight later, if no reaction, by 10 c.c. of A.M.P.[1] Thereafter A.M.P. can be repeated at about monthly intervals according to the amelioration of symptoms and tendency to relapse. After six doses the patient is instructed to return for an injection when required.

---

[1] Both preparations are put up by Messrs. Allen and Hanburys in 100 c.c. rubber-capped bottles with 0·5% phenol, ready for use.

The joint can be injected from the side, from the back, or from the front. Of these the anterior approach seems to be the easiest, the least painful and also the more certain. The surface marking which was drawn on the thigh of the case shown is simple in the extreme. The femoral artery is marked on a line joining the symphysis pubis with the upper edge of the great trochanter. The needle is inserted vertically on this line an inch or so outside the artery. A local anæsthetic is not really necessary but the use of a fine procaine needle as a probe to test the thickness of the capsule of the joint, and whether the point meets with bone, cartilage or tender synovial membrane, is a help.

When bone is encountered the injection can still be given provided that the needle has a sufficiently short bevel to drive the solution in between the closely apposed layers of the synovial membrane.

In a small proportion of cases, fluid is present in the joint so that it is as well to try aspirating with an empty syringe before attaching the syringe containing the solution.

Grant Waugh advises infiltrating the tissues in the neighbourhood of the joint. I do not do this intentionally, though the effect seems to be quite satisfactory as long as the point of the needle is inside the capsule. No surgical accidents have occurred.

We have now carried out many hundreds of these intra-articular injections of the hip-joint at the Clinic and I can therefore speak with some confidence of their value. I cannot claim that these alone will arrest the progress of osteo-arthritis of the hip-joint, because all cases arc given vaccine therapy as a routine. In addition, special exercises are given for stretching the adductors of the thigh, counteracting flexion and eversion deformities and strengthening atrophied muscles.

Over the last twenty-five years comparative skiagrams have demonstrated arrest of the disease process in a high proportion of cases, but since the introduction of acid phosphate injections, some joints seem positively to have improved as in the case of the patient shown to the meeting.

[Lantern slides were put on the screen, and skiagrams shown of a joint injected with a contrast medium.]

Osteoid-Osteoma of Upper End of Ulna.—D. Wainwright, F.R.C.S.Ed.

Early in February 1944, Jessie E., an unmarried girl of 18, employed in a pottery, was referred with a history of pain and increasing stiffness of the left elbow, which she first noticed fourteen months previously. She had been treated as a case of monarticular arthritis, with myocrysin, following an X-ray examination in April 1943 which did not show any bone abnormality.

She was complaining of intermittent pain in the left elbow-joint, which had been gradually getting worse and which troubled her at night and was aggravated by use of the joint. There was no history of injury.

Examination revealed an appreciable thickening of the upper end of the ulna with some tenderness on deep pressure; no local redness or heat. Movements of the elbow-joint were limited to about 45 degrees of extension and 30 degrees of flexion. W.R. was negative. B.S.R. 4 mm. in first hour. Blood-count normal.

X-rays: Considerable thickening and sclerosis of the upper end of the ulna with a well-defined lesion involving the articular surface, showing considerable mottled calcification and surrounded by a faint translucent line of demarcation.

The possibility of this being an example of an osteoid-osteoma was considered, but the tumour—if such it was—appeared to be very inaccessible, and she was kept under observation for some time. Her pain, however, persisted, and in an effort to relieve this a simple linear osteotomy of the upper end of the ulna was performed.

In spite of some temporary relief her pain returned and she was slowly becoming more disabled; she had to give up her work and was constantly losing sleep because of the pain at night. Movements of the joint were also more limited and, in July 1945, she had only about 10 degrees of extension and 20 degrees flexion of the joint.

In view of the inaccessible position of the lesion, the only prospect of cure appeared to be excision of the upper end of the ulna and reattachment of the triceps tendon to the shaft of the ulna. It was realized that removal of such an amount of the joint surface would give rise to some permanent weakness of the arm; but, in view of the persistent pain and increasing stiffness of the elbow—and also because as a result of such treatment a tumour, the nature of which was uncertain, would be removed—this treatment was decided upon.

On 27.9.45 a subperiosteal excision of the upper end of the ulna was performed, with some difficulty owing to the sclerotic nature of the bone, and the triceps tendon was firmly reattached to the upper end of the ulna.

Her progress was satisfactory but restoration of movement was rather slow; subsequent X-rays showed some forward subluxation of the head of the radius, and this was excised about ten weeks later. With active exercises the movement slowly increased and she now has only occasional aching in the joint after using it a good deal. The range of movement has continued to increase and, at the moment, she has about 80 degrees extension, 30 degrees flexion, full supination and 50 degrees pronation. Three months ago she resumed her old job for the first time for about twelve months.

Dr. McCall (Pathologist to North Staffordshire Royal Infirmary) reported that the tumour corresponded very closely to Jaffe's osteoid-osteoma, and his opinion was supported by Professor Turnbull of London Hospital.

The sections show the tumour to be well demarcated from the surrounding spongiosa and separated from it by a characteristic narrow zone of delicate fibrous marrow. The tumour itself consists of very atypical osteoid tissue and bone and corresponds in every way with the tumour described by Jaffe and Lichtenstein in their article in the *Journal of Bone & Joint Surgery*, 1940, **22,** 645.

Treatment of Displacements of the Distal Radio-ulnar Joint.—F. P. FITZGERALD, F.R.C.S.

Forward, backward and upward displacements of the radio-ulnar joint have been described. The following cases demonstrate methods of treating backward and upward displacements.

Backward displacement.—CASE I.—The patient, a female, aged 23, came to hospital in 1942 complaining of marked weakness of the right wrist. She had fallen on to the outstretched hand two years previously. On examination she had an obvious backward displacement of the distal radio-ulnar joint, which was confirmed by X-ray (fig. 1).

Treatment.—The dislocation was reduced by simple supination of the fore-arm, and this was verified by X-ray (fig. 2). The elbow and wrist were then immobilized in plaster of Paris in the supine position (*see* fig. 197, McNeill Love's "Minor Surgery," London, p. 374).

Some years previously I had treated a similar case in this fashion, which I had kept immobilized for three months. The result was good, but some backward displacement of the joint recurred some time later. The case being described was, therefore, kept in plaster for nearly six months. It was many months before full

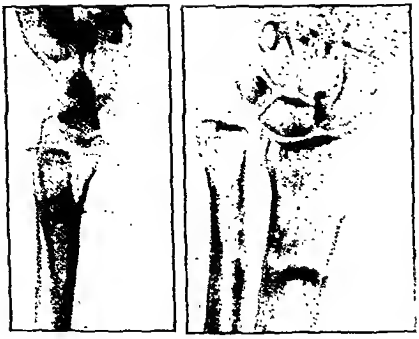

A B

FIG. 1.

A—shows the backward displacement of the head of the ulna. B—demonstrates the wide gap in the distal radio-ulnar joint.

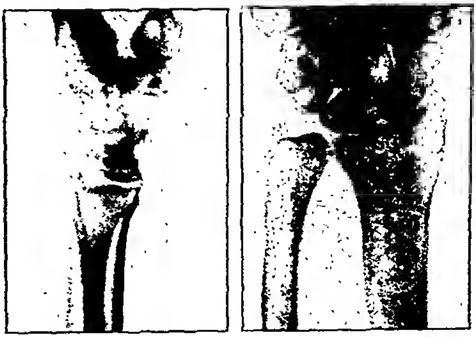


FIG. 2.

Both views show that the dislocation has been reduced.

pronation was recovered. Now the patient has a full range of movement, and the function is normal.

Upward displacement.—CASE II.—A female, aged 18, sustained in 1943 a compound fracture of the radius as the result of enemy action. There was extensive laceration of the soft tissues. The wound became infected and a large fragment of the radius sequestrated. When seen one year later there was a large gap between the fragments of the radius, and the distal radio-ulnar joint was dislocated upwards (fig. 3). Instead of excising the lower end of the ulna it was decided to attempt a closed reduction. Consequently, Kirschner wires were passed through the metacarpals and olecranon, and Cuendet's distraction apparatus fixed to the Kirschner wires. The distraction on the radial side was then increased by means of the

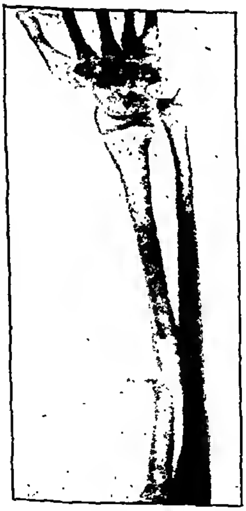


FIG. 3.

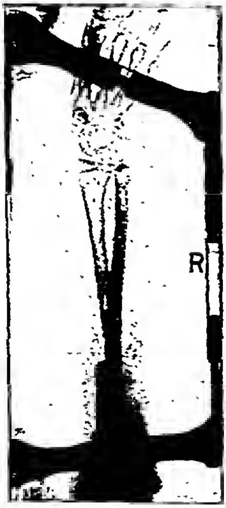


FIG. 4.

FIG. 5.

FIG. 3.—Ununited fracture of radius with upward displacement at the radio-ulnar joint.

FIG. 4.—Cuendet's apparatus fixed to Kirschner wires in olecranon and metacarpals. The dislocation has been corrected.

FIG. 5.—The grafts are firm. The length has been maintained.

turnbuckle and the dislocation thus reduced (fig. 4). The distraction apparatus was left in place and the radius grafted by means of onlay and chip grafts through a posterior approach. When the plaster was removed the grafts were found to be firmly united (fig. 5).

Present condition.—The patient is doing full work as a clothes presser and her forearm and wrist are normal in every way.

CASE III.—A bricklayer, aged 36, sustained in 1945 a compound fracture of the radius and ulna. The wound became infected, and, as in the previous case, a large sequestrum was extruded. When seen one year after the injury, there was non-union of the radius and a distal radio-ulnar dislocation (fig. 6). Cuendet's apparatus was again applied and the dislocation gradually reduced (fig. 7). As before the radius was exposed through a posterior approach and it was fixed by chip and onlay grafts (fig. 8). The ulna was found to have united. Now three months after removal of the plaster he has 15 degrees limitation of pronation and 15 degrees limitation of extension of the elbow-joint. Flexion is full. The grip is not yet quite normal. He is back at light work and he says that the function of the limb is gradually improving. The bones have united and the dislocation has been reduced (fig. 9).

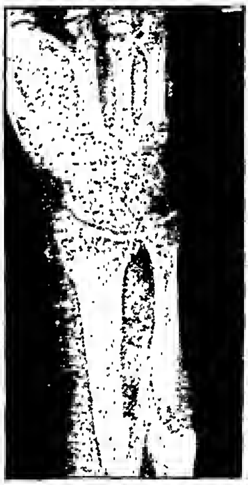


FIG. 6.

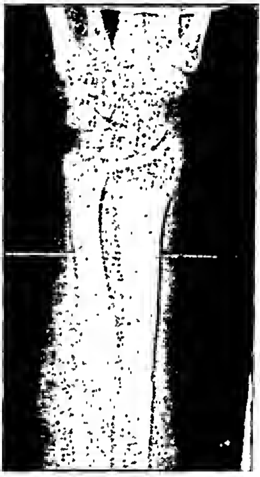


FIG. 7.

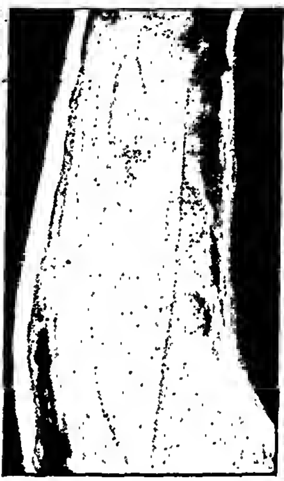


FIG. 8.

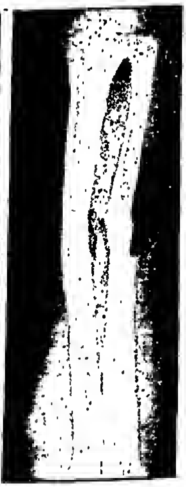


FIG. 9.

FIG. 6.—The radius is displaced upwards at the distal radio-ulnar joint.

FIG. 7.—The dislocation is being gradually corrected by the distraction apparatus.

FIG. 8.—The dislocation has been corrected. The radius has been grafted. The limb is still in plaster.

FIG. 9.—Three months after operation. The graft is firm; the length has been maintained.

CASE IV.—A schoolgirl, aged 14, sustained in 1942 a fracture of the lower end of the radius. When seen a few months ago there was marked radial deviation of the hand (fig. 10), and the head of the ulna was very prominent. She complained of marked weakness of the hand. In this case an osteotomy was performed on the lateral side of the radius, and the lower end of the ulna was excised. The line of the osteotomy was then "opened out" (fig. 11), and the excised piece of the ulna was used as a buttress graft (fig. 12).

POSTSCRIPT.—Function is now normal, seven months after operation.

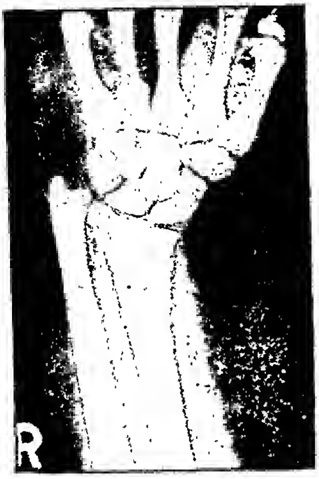


FIG. 10.

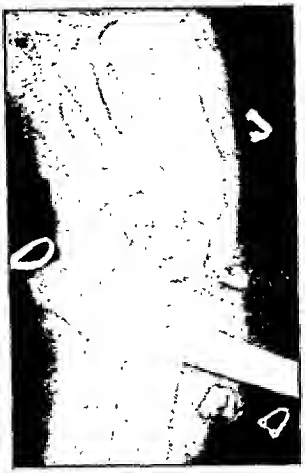


FIG. 11.

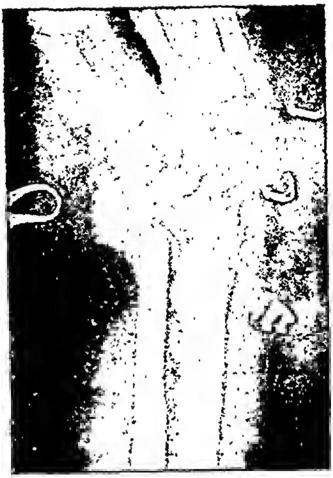


FIG. 12.

FIG. 10.—Displaced joint; deformed radius; no manipulative correction possible.

FIG. 11.—The lower end of the ulna has been divided. An osteotomy has been performed on the radius and "opened out" by the width of the osteotome.

FIG. 12.—The lower end of the ulna has been shaped to fit the osteotomy gap. The alignment of the joint has been restored.

Chondro-osteodystrophy. ? Morquio.—J. A. CHOLMELEY, F.R.C.S.

J. B., born 17.10.44.

10.11.44: Noticed to have mild talipes equinovarus; treated by manipulation and application of Denis Browne splints. Good correction obtained.

10.9.45: Noticed to have lumbar kyphos.

1.10.45: Admitted to Royal National Orthopædic Hospital, Stanmore.

On admission.—Head: Anterior fontanelle widely open. Face: Suggests gargoyle type. Spine: Dorsolumbar kyphos. Feet: Satisfactory correction of equinovarus.

Treatment.—Spinal frame, followed by spinal support.

Investigations.—Mantoux: 1/10,000 and 1/1,000 negative. B.S.R.: 2 mm. in first hour. W.R. negative. Blood cholesterol: 130 mg. per 100 c.c. W.B.C.: 6,100 per c.mm., polys. 59%, lymphos. 40%, monos. 1%.

X-rays.—Spine: Anterior "dislocation" of D.12 on L.1 with "bite" out of antero-superior surface of body of L.1. Several of the dorsal vertebral bodies are pear shaped but show none of the anterior tongue typical of Morquio's chondro-osteodystrophy. Intervertebral spaces normal. Hips: Acetabular roofs very sloping; femoral necks broad and almost vertical. Slight upward displacement both femoral heads. Forearms: Radii thick and "shapeless". Humeri: Broad and straight.

Epiphyses.—Dates of appearance: Lower end humerus, capitellum usually appears at 2 years, in this case present at 1 year. Lower end radius normally appears at 2 years, in this case present at 1 year. Carpal ossification normal in this case at 1 year. Tibia and fibula lower ends usually appear at 2 years, in this case present at 1 year. Tarsal ossification, normally four centres at 1 year, in this case five centres present.

Osteo-arthritis of the Trapezio-metacarpal Joint treated by Excision of the Trapezium.—W. H. GERVIS, F.R.C.S.

Osteo-arthritis of the trapezio-metacarpal joint is fairly common, and when at all severe is a painful and crippling condition. I have been treating this condition by excision of the trapezium for a number of years.

CASE I.—Female, aged 53. Complained of pain in the base of both thumbs on use. X-ray showed osteo-arthritis of trapezio-metacarpal joints, right and left.

Operation November 1945, excision of right and left trapezium.

She is very satisfied with the result. There is no apparent deformity and she can use her hands normally, but with a very slight loss of power in the thumbs.

CASE II.—Cowman, aged 48. Complained of pain in base of right thumb and was unable to work. X-ray showed osteo-arthritis of trapezio-metacarpal joint.

Operation September 1946, excision of right trapezium.

Was able to start milking within a month of operation and is now milking 20 cows a day.

The following cases were also shown:

(1) **Multiple Disseminated Calcinosis.** (2) **Congenital Deformity of Lumbar Vertebræ with Sciatic Nerve Lesion.**—W. D. COLTART, F.R.C.S.

(1) **Degloving Accident to Right Fore-arm, Followed By Necrosis of Skin Flaps, &c.** (2) **Degloving Accident to Left Lower Leg, Treated By Immediate Full-Thickness Grafts Obtained from the Skin Flaps.**—K. I. NISSEN, F.R.C.S.

[*February* 4, 1947]

DISCUSSION ON PAIN IN THE UPPER LIMB, EXCLUDING SHOULDER LESIONS

Dr. Wilfred Harris: I propose to limit my remarks to lesions of various kinds affecting the nerves and nerve roots supplying the hand, arm, and shoulder girdle.

Median nerve.—Atrophy of the thenar eminence, abductor and opponens pollicis, without interosseal atrophy, may occur in rheumatoid arthritis of the trapezio-metacarpal joint. This may be a source of considerable pain on the outer side of the wrist, with obvious swelling of the joint, and weakness and pain on movement of the thumb. R.D. on electrical tests may then be found in these muscles. When the interossei, especially the first dorsal interosseous, show wasting in addition, the lesion may be rib pressure on the first dorsal nerve, or it may indicate an acute or chronic anterior poliomyelitis, or syringomyelia, or an intramedullary tumour at the first dorsal level. Pain is sometimes a feature in acute poliomyelitis, especially in older subjects. In syringomyelia and intramedullary tumours pain may be a marked feature, while sensory changes will be distinctive, especially loss to pain and temperature.

Even without noticeable heavy use of the hand the lower portion of the median nerve may suffer severely from a pressure neuritis in the carpal tunnel, where it lies between the palmaris longus and the flexor carpi radialis. Russell Brain (*Proc. R. Soc. Med.*, 1946, **40**, 83) described this syndrome fully and its treatment. Pain like "electricity" in front of the wrist and outer half of the hand is complained of, and wasting of the thenar eminence and median nerve anæsthesia are found.

Injuries of the median nerve in the region of the elbow are becoming increasingly common with the more frequent use of parenteral injections, and especially in intravenous injections. Using the median basilic vein the needle may pierce the median nerve beneath the vein, and injections of drugs and of dyes used in renal and gall-bladder investigations have caused irreparable damage from severe median neuritis. Even worse is the result of injecting the brachial artery instead of the vein, when injecting a dye, as gangrene of the hand has been caused in this way. These dangers can be almost wholly avoided by choosing the median cephalic or the cephalic vein for intravenous medication.

Gunshot and stab wounds involving the median nerve, if clean, may give rise to no pain, but septic wounds involving the nerve cause prolonged pain in the hand, with median type of wasting and anæsthesia and glossy skin. Median *causalgia,* very common in the first World War, usually resulted from slight wounds of the median above the elbow. Mostly the muscular wasting and anæsthesia were slight, though the subjective burning pain and hyperæsthesia which might be started by the slightest stimuli, such as vibration of the floor, were often intense.

A not uncommon form of chronic *ulnar neuritis* is associated with frequent subluxation of the ulnar nerve from the groove at the back of the inner condyle, or from progressive filling up of this groove, causing pressure on the nerve, so that flexion of the elbow becomes increasingly uncomfortable and painful as the years go by. This may ultimately become so troublesome that surgical intervention may be necessary to bring the nerve forward to the front of the elbow by dividing the inner head of the flexor carpi ulnaris. Perineuritis of the *radial nerve* may result from a heavy muscular strain, as from lifting a patient from a trolley on to an operating table. Aching pain in the arm and back of forearm results, which is aggravated by such movements as stooping with arms extended, as in lacing the shoes. Massage should be avoided in these cases, and usually there is no detectable wasting or anæsthesia, though the triceps-jerk may be lost.

General *brachial neuritis* from chill, exposure to draught, rheumatism or influenza, may cause the most acute pain in the limb, with resulting sleeplessness, lasting for several weeks. There is considerable tenderness above the clavicle and over the nerve trunks in the arm, with hyperæsthesia, the slightest movement being extremely painful. Partial immobilization is essential, though patients cannot bear plaster splinting as in sciatica, and adhesions in the shoulder-joint are a frequent sequel, and may require wrenching afterwards under an anæsthetic. These are probably due partly to the lack of movement, and partly to the trophic effects of the neuritis. Usually complete recovery takes place, though management and nursing of the patient may be most difficult. Sometimes periarticular adhesions in the wrist and finger joints, and glossy skin may result. These complications are more likely to occur in extension of inflammation upwards from the apex of the lung and pleura in tuberculosis or from involvement of the cervical roots by growths in the neighbourhood of the spinal foramina.

Of recent years symptoms of brachial neuritis have been recognized as produced by rupture or dislocation of an intervertebral disc, usually the sixth or seventh cervical. The onset of the pain may be gradual or sudden, and may be so severe as to require continuous treatment with morphia for a few days. It may be mistaken for tennis elbow, and the condition may become more or less chronic, with varying symptoms for years, the pain being aggravated by use of the arm, or by lying on that side. Occasionally the slipped disc may press upon the spinal cord and cause paraplegia, temporary or permanent.

In spite of the enthusiasts for the newer teaching not all cases with brachial neuritis are due to disc lesions.

Posterior or long thoracic neuritis may result from direct chill, as from a down draught from a window close to the bed, causing typical winged scapula, with aching pain in side of neck and over scapula, and down outer upper arm. Similar results may follow toxic neuritis after influenza or paratyphoid. Excessive muscular action of the scalenus medius may damage the nerve as it passes through the muscle on its way to the serratus, as I have seen in a man who developed serratus palsy immediately after a swimming race, in which he used the side stroke. The winging of the scapula is characteristic, with inability to raise the arm beyond the horizontal.

Trapezius palsy may be easily mistaken for serratus palsy, owing to the partial winging of the scapula. This is seen best with the arm at rest and the hand resting on the hip. The winged appearance disappears at once on holding up the arm by the undamaged serratus (*see* figs. 4 and 5). In trapezius palsy the vertebral border of the scapula lies further from the mid-line than its fellow, and the action of the serratus is normal.

Posterior scapular neuritis (the nerve to the rhomboids) may result from direct wounding, or from excessive muscular action of the scalenus medius and levator anguli scapulæ. I have seen it produced by heavy heaving efforts in digging a deep grave. Sudden pain at the back of the neck and shoulder, with weakness of the arm, produced typical palsy of the rhomboids and levator anguli scapulæ. As a result the scapula hangs lower than its fellow, with the inferior angle everted (*see* fig. 7). [The figures referred to may be seen on pp. 69 and 71 of Dr. Harris's book "Neuritis and Neuralgia," London, 1926.]

Mr. David Le Vay: When pain is referred from a lesion in the posterior triangle or cervical spine there is an obvious analogy with low back pain and sciatica. In both regions we have to consider congenital bony anomalies; intrinsic neuritis; spastic muscles (piriformis or scaleni); and prolapsed intervertebral discs. The sciatica problem has been solved almost exclusively in terms of the prolapsed disc. But a simple solution is impossible in the upper limb because of the several factors involved—the mobile shoulder girdle, the dependent arm, and the overriding clavicle. The diagnosis of brachial neuritis, however, appears increasingly ill-founded as the importance of mechanical factors emerges.

(1) POSTERIOR TRIANGLE SYNDROMES

These are essentially postural in origin, and in nearly every case there is more than one postural mechanism at work. As Professor H. A. Harris says of the ulnar nerve, the neurovascular bundle of the arm "lives dangerously" in its passage from thoracic outlet to axilla, and this is due to imperfect adaptation to the erect position. It is subject to a normal variation in anatomical relationships which easily verges on the pathological. Thus, Falconer and Weddell (1943) have shown in connexion with costoclavicular compression that many normal individuals can obliterate their radial pulse by backward bracing of the shoulders.

(*i*) *Syndrome of the "normal" first rib.*—"Normal" is often a misnomer as developmental asymmetry is common. As gravity drags on the dependent arm the bundle is stretched over the outer border of the bone, a movement which can be visibly reproduced at operation. The tendency is increased by carrying heavy burdens, hence the preponderance of right-sided symptoms. Symptoms appear when the tone of shoulder-girdle musculature is reduced by fatigue, and the scapula gradually descends. This descent is the most important and constant of all mechanical factors at work, and also forms the background to the other, possibly more striking, posterior triangle syndromes, e.g. costoclavicular compression. Clinical features at their most severe are those classically ascribed to cervical rib; at their mildest they are those known as acroparæsthesiæ.

It must be recognized that *acute* descent of the shoulder girdle may be caused by trauma, with intense pain and swelling in the whole limb, and I have seen this in two patients whose right arms were trapped and forcibly depressed. Severe persistent pain and paresis followed, with gross œdema, and sagging of the right scapula. Both were completely relieved of pain and swelling by resection of the first rib, and in one an abundance of new venous channels in the posterior triangle made it clear that thrombosis of the subclavian vein had occurred. Such cases link up on the one hand with "strain thrombosis of the axillary vein", and on the other with traction injuries of the brachial plexus.

(*ii*) *Syndrome of costoclavicular compression.*—Though the clinical picture is often striking, there is usually some associated sagging of the shoulder girdle. The narrow costoclavicular gap is further closed in abduction and elevation of the arm. Pain is elicited by raising the arm, or bracing the shoulders in the attention position, or at night when the clavicles fall backward. The distinctive features are due to clavicular pressure on the *whole* plexus, with possible sensory disturbance over the entire limb surface, and on the subclavian vein. The position of exacerbation may produce venous stasis, œdema, distension of pectoral collaterals, and widening of the axillary venous trunk which may be visualized by contrast media.

Walshe, Harvey Jackson and Wyburn-Mason discuss the constant movement of the costoclavicular vice with every respiration and change of position, and the diffuse fibrosis of intervening connective tissue which may result. This mass of scar tissue may be seen at operation and is capable in itself of maintaining symptoms by its constricting action.

(*iii*) *Scalene syndrome.*—Leriche (1946) believes that the artery and plexus may be compressed in the gap between scalenus medius and anterior. It is certainly better to think in terms of this gap than of a probably hypothetical scalenus anterior syndrome. Walshe and his colleagues (1944) pointed out that isolated spasm of this latter muscle is not only improbable, but would not compress the bundle against the first rib even if it did occur. Clinical tests designed to elicit and isolate this muscle's action are unsatisfactory since they also alter the relationships of clavicle, bundle and first rib. Though benefit often follows anterior scalenotomy, this is because of relaxation of one limb of the scalene gap and possibly because of some change in costoclavicular apposition; in some cases the operation causes severe exacerbation. There is much more evidence compromising the scalenus *medius*, against the knifelike anterior edge of which the clavicle can certainly squeeze the neurovascular bundle. Therefore it seems advisable to discard the term "scalenus anterior syndrome", and to refrain from dividing this muscle without clear indication just because the operative procedure is simple.

Cervical rib.—The problem of cervical rib is largely solved in terms of the three syndromes already discussed. Though one agrees with Eden (1939) that a large rib thrusting itself into the scalene gap must be removed, these cases are rare. The often severe clinical disturbance associated with the usual rudimentary ossicles can hardly be due to the ribs themselves or to any fibrous band. X-ray usually reveals a general asymmetry in which the cervical rib is important only as an index that the first thoracic rib is abnormal in position and in its relation to the clavicle. Symptoms are still due to drag over the first rib, or compression between first rib and clavicle or in the scalene gap. Leriche points out that cervical rib affords an additional origin to the scalenus medius which enables that muscle to encroach still further on the scalene interval.

Treatment.—Conservative measures are adequate for most cases; but, if operation has been performed, physiotherapy and muscular re-education must be continued as the bundle is liable to drag even when the first rib fulcrum has been removed. Operation should not be delayed too long in presence of severe pain. Not only do neurotic complications appear, but, once established, well-marked wasting and hypoæsthesia are only slowly reversible. Partial resection of the first rib is advocated as a routine for severe cases. Since this procedure necessarily entails division of the scalenus anterior, erasion of the insertion of scalenus medius backwards, and removal of the bony ledge of rib behind the neurovascular bundle, it deals with all the factors in the complex pathology. General anæsthesia is desirable, and most of the bone can be removed through a straight incision paralleling the clavicle. The operation is tedious and may be difficult, and it is fortunate that the thoracic duct is a left-sided structure.

(2) Prolapse of Cervical Intervertebral Discs

Once the clinical picture becomes familiar this condition is found to be not much less common than the posterior triangle syndromes as a cause of pain in the arm. There is a combination of orthopædic signs in the neck—pain and restriction of extremes of motion—with radicular neurological features in the arm, in which pain is often more of the nature of unpleasant paræsthesiæ.

The disc at C.5-6 irritates the sixth cervical root, causing wasting of the biceps and pain over the dorsum of thumb and index. The disc at C. 6-7 compresses the seventh root with triceps wasting and more extensive sensory disturbance spreading to the back of the middle finger. The picture is not always so clear-cut; severe wasting of the deltoid is sometimes seen. Patients are often most unhappy at night, for the pillow presses on the back of the head, which they prefer to allow to hang backwards. Unlike the situation with lumbar prolapses, the X-ray here is of constant value. One expects to see the narrowed intervertebral space, with bony proliferation at the anterior margins of the bodies and in the region of the foramen.

Conservative treatment deals with most cases, and operation is usually left to the neurosurgeon, but I should like to stress the value of manipulation. The long-term results of manipulation of the spine for sciatica are disappointing because of the continued action of body-weight. This is much less important here, and manipulation of the neck under anæsthesia often gives gratifyingly persistent improvement. As with lumbar manipulation, there is little risk of exacerbation if the spine is not flexed but subjected only to rotation and hyperextension.

REFERENCES

Eden, K. C. (1939) *Brit. J. Surg.*, 27, 111.
Falconer, M., and Weddell, G. (1943) *Lancet* (ii), 539.
Leriche, R. (1946) *Pr. méd.*, 41, 569.
Walshe, F. M. R., Jackson, H., and Wyburn-Mason, R. (1944) *Brain*, 67, 141.

Dr. Frank A. Elliott: I shall say nothing about the better-known inflammatory, neoplastic, and traumatic causes of pain in the arm, but will deal briefly with the more controversial aspects of the subject.

Herniation of the fifth and sixth cervical discs is a common cause of pain in the arm and upper chest. It radiates from the back of the shoulder girdle, down the back of the arm, and along the radial border of the forearm to the wrist, and is often felt in the upper part of the pectoralis major and over the scapula. It is aggravated by movements of the head, by pressure on the head, and sometimes by certain movements of the arms. Tingling is felt in the thumb (sixth root) or index and middle finger (seventh root), and slight sensory loss may be present in these situations. Weakness and slight wasting may occur in triceps and the extensors of wrist and fingers. "Trigger" points are often present in the shoulder girdle and pectoralis major; when pressed upon, pain and tingling shoot down the arm, and if these points are infiltrated with novocain, relief from pain is obtained. Depression of biceps and triceps reflexes occurs in lesions affecting the sixth and seventh roots respectively. In doubtful cases, contrast myelography will demonstrate the level of the lesion.

The costoclavicular syndrome is also common. Drooping of the shoulder, or elevation of the uppermost rib (as in scoliosis), causes pressure on the lower cord of the plexus as it passes over the rib into the axilla, and exposes the subclavian artery to nipping between the clavicle and the first rib in certain positions of the shoulder.

Attrition at this site may lead to a reactive fibrosis around the plexus and aneurysmal dilatation of the artery, with or without thrombosis. Six types of sensory symptoms are encountered, in varying combinations: "Pins-and-needles" of ulnar distribution, due to irritation of the lower cord of the plexus; "pins-and-needles" in the entire hand, due to compression of the plexus as a whole; an unpleasant sense of numbness in the limb, due to compression of the subclavian artery, when the arm is maintained in positions which cause compression of the artery; ischæmic muscle pain, sometimes severe, from subclavian thrombosis; pain in the trapezius associated with the postural strain of a drooping shoulder; and finally, pain behind the clavicle and down the inner aspect of the arm and forearm from pressure on the plexus. Objective neurological and vascular signs are too well known to require recapitulation here.

Extramedullary spinal tumours can give rise to root pain in the arm for months before sensory, motor, or reflex abnormalities appear. The pain is sometimes abrupt in onset, remittent in course, and apparently relieved by manipulation, physiotherapy, and peripheral injections of novocain—misleading features which may suggest other diagnoses. Paræsthesiæ in the hand indicate that the lesion is somewhere along the afferent pathways, and the simultaneous presence of tingling, coldness, and "heaviness" of the legs suggests that the lesion is intraspinal. Neurological examination and lumbar puncture should be repeated from time to time, and contrast myelography is needed for suspicious cases.

Syringomyelia, infective radiculitis, and post-herpetic neuralgia are not uncommon sources of pain in the arm, but to remember them is to recognize them.

Cervical osteo-arthritis sometimes gives rise to root pains in the limbs. In some, an osteophyte is radiologically demonstrable in the intervertebral foramen corresponding to the affected root. In others, there is no such evidence, but there is reason to suppose that the root sheath is involved by inflammation from the adjacent intervertebral joint. Symptoms differ from those of a prolapsed disc in four respects. Pain has often a burning quality. Pain and paræsthesiæ are often more widespread, indicating simultaneous affection of more than one root. Objective neurological signs of root compression are seldom present. Finally, there are, or have been, symptoms elsewhere from osteo-arthritis at other levels of the spine and in the proximal joints of the limbs.

Subacute muscular rheumatism following rheumatic fever or its equivalents can give rise to transient pain in the arm. There is always a history of similar pain having occurred in other parts of the body in previous attacks, and objective neurological signs do not occur. Pain limited to one part of the body in successive attacks should not lightly be attributed to this condition. Spondylitis ankylopoietica is a rare cause of pain in the neck and arm; in the course of time, rigidity of the spine, a raised sedimentation rate, and the characteristic radiological changes in the spine and sacro-iliac joint will disclose the nature of the disease.

Fibrositis and brachial neuritis are often diagnosed, but there is as yet no pathological proof of their existence, and it has been my experience that cases so labelled usually turn out to be something else if they are followed up long enough. Moreover, so many cases of prolapsed discs, spinal tumours and spinal osteo-arthritis give a history of having been treated for fibrositis in the early stages of the disease, that it may be inferred that the clinical features of fibrositis and neuritis are not free from ambiguity.

Dr. J. W. Aldren Turner: The name "thoracic inlet syndrome" is a poor one to comprise the various conditions which cause compression of the brachial plexus and great vessels as they pass out from the neck into the axilla; a more correct name anatomically would be "cervical outlet syndrome", or better "axillary inlet syndrome", as the compression is not directly related to the thoracic inlet.

Surgical treatment is very rarely necessary for lateral prolapse of the C.6-7 intervertebral disc, the great majority of patients become free of symptoms with rest in bed, with three or four pillows to keep the neck flexed and a sling on the affected arm and analgesics in the early stages. The usual course is for the pain to be completely relieved in three to four weeks, though paræsthesia in the index finger may persist for several months and the triceps-jerk remain absent. This prognosis is based on 35 cases with the typical clinical picture, though the diagnosis was not proved by myelography in any of the cases.

The condition variously described as "infective neuritis of the shoulder girdle" (Spillane, 1943) and "acute brachial radiculitis" (Aldren Turner, 1944) may cause severe pain in the shoulder and upper arm before a flaccid palsy suddenly appears. The palsy usually comes on three to four days after the pain subsides, but in a few cases pain has persisted for several weeks before the onset of paralysis. The paralysis is a lower motor neurone one and at times sensory impairment is present in addition. There is no constitutional disturbance and the C.S.F. was normal in the cases where it has been examined.

REFERENCES

SPILLANE, J. D. (1943) *Lancet* (ii), 532.
TURNER, J. W. ALDREN (1944) *Brit. med. J.* (ii), 592.

Mr. W. E. Tucker: It is difficult in some cases of acroparæsthesia to be certain whether the symptoms start in the shoulder and move down the arm, or in the hand and work up the arm to the shoulder and neck muscles. Often two main groups are seen, one in younger patients with drooping shoulders, the other type in older patients with a raised shoulder and contracted cervical muscles, especially the trapezii. Often this latter type are found to have osteo-arthritis of the cervical spine, and owing to a jarring injury such as may occur in taking a divot on hard ground while playing golf, the lower cervical joints are traumatized and symptoms start. If the symptoms start in the hand, the forearm flexors are found contracted, there is pain referred to the intrinsic muscles of the hand and a tender point appears in the extensor origin of the wrist from the external humeral epicondyle and radio-humeral collateral ligament. Often this type shows itself in young girls starting employment such as nursing, or housewives, who are continually lifting or carrying articles. As one writer has said: "Life is now one continual grip for the housewife." Most cases improve with rest from strain, remedial exercises, combined with gentle manipulation of the neck and faradic contractions of the muscles of the arm, shoulder and neck. The patient should be given advice with regard to carrying parcels and shopping bags, relaxing the hands while sleeping and arrangement of four pillows at night, so as to support the head and neck.

Section of Dermatology

President—SYDNEY THOMSON, M.D.

[*February* 20, 1947]

Granulosis Rubra Nasi.—D. I. WILLIAMS, M.B. (for SYDNEY THOMSON, M.D.).

J. P., aged 9 years 11 months.

His mother complains of his red, sweating nose. He himself is little concerned about it or inconvenienced by it. The red area on the nose is said to have been present since birth. The sweating is more marked in hot weather. The peripheral circulation elsewhere seems to be normal. There is no excess sweating elsewhere on the face or body. He has one sister, aged 3, with a normal nose. There is no family history of any similar condition.

The tip of the nose, the alæ nasi and a projection in the mid-line up to the bridge of the nose are symmetrically red; the edge of the lesion fades off into normal skin. On diascopy a brownish-yellow colour is seen diffusely throughout the affected area. There is a certain amount of telangiectasia and a few pinhead brownish macules.

Prominent over the tip of the nose are small, tense, round vesicular lesions of a bluish tint with central dark areas; these hidrocystomata are about half a dozen in number and were far more numerous when he was first seen in the Out-patient Department of King's College Hospital in the autumn of 1946. Small beads of sweat can be seen collecting in the affected areas. These turn red litmus paper blue.

X-ray of chest and antra: No abnormality.. E.N.T. report: Normal, no signs of infection in ear, nose or throat. Mantoux reaction: 1/10,000 negative. Gastric residuum: *Before histamine.*—Reaction acid; free HCl 31 c.c. N/10; total acid 42 c.c. N/10. *After histamine.*—Reaction acid; free HCl 67 c.c. N/10; total acid 77 c.c. N/10.

Dr. F. Parkes Weber: If this is really a specimen of what is usually termed granulosis rubra nasi, is it right to call it a granulosis? It makes me think of a nævoid condition. This is suggested by the position and by the fact that it has remained since birth always the same. "Granulosis" would seem to imply some granulomatous condition or some growth of granular tissue. The history and the position in the middle line make one think of some form of nævoid (chiefly vascular) developmental abnormality.

The President: The name, of course, was given to the condition by Jadassohn in 1901 when he wrote his monograph. Granulomatous lesions have not been found histologically except in one case where a certain number of giant cells were found.

Poikiloderma Congenitale (Thomson). Two Cases.—C. H. WHITTLE, M.D.

CASE I.—N. S., a boy, aged 12 years.

History of discoloration since birth of the skin of face, forearms, hands, legs and feet. The face shows a telangiectatic reticular vermilion pattern, with pale skin between the meshwork. Both cheeks and ears are involved. The condition is similar though less marked on the forearms and lower legs. There is scattered brown pigmentation also. Scars present are the result of numerous boils. In addition there is a marked tendency to warty hyperkeratoses on the knuckles and on prominences such as the elbows, knees, malleoli and heels. He has sandy hair, brown eyes and a triangular-shaped head with the apex corresponding to the chin. He is thin and rather small for his age but intelligence appears normal. *Family history* shows no others affected, but the mother's father had eczema. Two siblings (girls) aged 7 and 9 are unaffected.

Remarks.—The condition corresponds in many respects to Thomson's description of 3 cases all in girls (Thomson, S., 1935, *Brit. J. Derm. and Syph.*, **48**, 222), notably in appearance, shape of head and history of early onset, but differs in the tendency to hyperkeratosis on prominences. The buttocks are not affected.

Vitamin-A content of plasma (by courtesy of Dr. T. Moore).—45 I.U. per 100 c.c. (25.11.46); 65 I.U. per 100 c.c. (14.1.47). Carotene 76 I.U. per 100 c.c. (25.11.46); 47 I.U. per 100 c.c. (14.1.47). (Normal vitamin A 70—120 I.U.) This low vitamin-A level may be significant.

CASE II.—G. S., a girl, aged 4 years.

The child was brought to the clinic because of the discoloration of the cheeks noticed soon after birth. There had been no previous swelling. The cheeks are the only parts which show the bright red (bluish-red in cold weather) reticular pattern, with circular islands between of normal pale skin. There is a tendency to scale and possibly slight superficial atrophy, like a glaze. There is a hint of similar discoloration of the skin of the upper lip. The buttocks are not affected.

The only noticeable abnormality elsewhere is a fairly general dryness of the skin amounting to mild xerodermia, affecting chiefly the outer aspects of the upper arms and of the thighs, with some follicular hyperkeratosis. She is chubby, and inclined to a bluish complexion when cold. Hair dark.

When first seen at the age of 1 year she showed well-marked koilonychia, an unusual feature in an infant. The nails are now normal.

The family history shows no hereditary features. Two siblings, a brother aged 6 months and a sister aged 13, are unaffected; nor is there any consanguinity.

Vitamin-A content of plasma (by courtesy of Dr. T. Moore).—Vitamin A 85 I.U. per 100 c.c. Carotene 131 I.U. per 100 c.c. (12.2.47).

Dr. F. Parkes Weber: I should like to know whether Dr. Whittle regards these cases of poikiloderma congenitale of Dr. Thomson as a kind of congenital or developmental dysplasia chiefly affecting the superficial blood-vessels. It seems to me that cases of this kind are in fact what I have suggested in regard to the previous case (granulosis rubra nasi), examples of congenital or developmental dysplasia mainly affecting the blood-vessels. This idea would, of course, fit in with occasional association of other developmental abnormalities.

The President: With regard to Dr. Whittle's first case (the boy aged 12), I was, of course, very delighted to see him as it is a classical picture, with a history since birth, or very soon after birth, of the development of a network of vessels and the atrophy over the vessels. As the child grows older the changes become more marked, and warty lesions develop later. One of my cases started to show that only at the age of 12. Dr. Dowling has shown one or two older cases, with the warty change very marked. I think that in the cases I have seen bone changes have always been present; the striking thing is the shape of the head; in one case there was maldevelopment of radius and ulna.

On the question of vitamin-A estimations: we were, of course, not doing these twelve or fifteen years ago when I first saw the cases. There seems to be no doubt it is a developmental defect; but it has certain peculiar features of its own. There are numerous instances in the literature of gross endocrine disturbances of varying types accompanying poikiloderma. I have not seen any obvious endocrine disturbances in these children; the only other abnormalities have been in the bones. I would like to have an opportunity of examining Dr. Whittle's second case (the girl aged 4) much more thoroughly and over a much longer period than the few minutes available at this meeting, but certainly the pattern, &c , of the cheek lesions strongly supports his diagnosis.

Dr. A. C. Roxburgh: I saw a case of Dr. Dowling's two years ago. The patient, an adult, was covered with warty growths and atrophic patches and was altogether in a most miserable state.

The President: Dr. Whittle has asked for suggestions as to treatment but I do not know of anything very satisfactory. We tried many treatments, and ended up with local electrolysis of the more obvious vessels on the face, but it was a very tedious business and obliterated only small areas.

Raynaud's Phenomenon, with Paroxysmal Hæmoglobinuria, Caused By Cold Hæmagglutination.—C. H. WHITTLE, M.D., A. LYELL, M.B., and M. GATMAN, M.B.

C. M., a married woman aged 56. History of attacks of blueness, tingling and numbness of the hands in cold weather for two years with occasional blood-stained urine. Anæmia present for five years.

The patient is a well-covered, pale, anæmic, slightly icteric, nervous woman. She has two children alive and well. Family history shows nothing of note. She does not smoke. Central nervous system normal. Heart slightly enlarged with apical presystolic and systolic murmurs. Arteries good. B.P. 150/90. No splenic or hepatic enlargement detected.

The lesions which appear only when extremities are chilled consist of bluish-red macules and blotches chiefly on the tips of thumbs, backs of fingers, and dorsa of hands, varying in diameter from 1 cm. to 2 or 3 cm. Tips of ears and nose are also slightly affected.

Diascopy suggests extravasation of blood, as colour does not disappear on pressure.

Laboratory findings.—Macrocytic anæmia of moderate degree which has not responded to iron or liver therapy. Platelets were increased and reticulocytes have averaged 5%. Sternal bone marrow shows a hyperplastic marrow essentially of the normoblastic type though nests of megaloblastic activity are present. Lymphocytes are definitely increased. Plasma bilirubin averages 1·8 mg. per 100 ml. and is of the indirect type. Cold hæmagglutinin titre 1 : 2,000,000. Erythrocyte fragility: (*a*) *saline*—normal at 39° C. and 23° C.; (*b*) *traumatic*—normal at 39° C.; increases in intensity at temperatures below 26° C.; very marked at 4° C. Sedimentation rate —6 mm. per hour at 39° C.; 44 mm. per hour at 23° C. Urine contained red cell ghosts and methæmoglobin after exposure of patient to cold. Urobilin increased: bile pigment negative: Bence-Jones protein negative. Histamine-test meal showed active hydrochloric acid production. Wassermann and Kahn (repeated) negative. Donath-Landsteiner reaction negative.

Dr. A. Lyell: The explanation of the colour changes in the extremities seems to be that the cooling gives rise to intravascular hæmagglutination, the blood flow in the capillaries ceases, the hæmoglobin becomes reduced: the colour remains on diascopy not because the corpuscles are extravasated but because they cannot be shifted in their clumped state within the capillaries.

Since, however, the hæmagglutination is reversible the flow starts again when the part is warmed: but at low temperatures owing to the increased mechanical fragility of the corpuscles some are hæmolysed, and this explains the slight icterus with raised serum bilirubin. It also explains the occasional attacks of hæmoglobinuria.

Treatment with liver injections has been followed by great improvement in symptoms, and she can withstand longer exposure and lower temperature without ill-effect. Though immersion of her hands in ice-cold water for half an hour will provoke an attack, recovery takes place now in twenty minutes. But a severe attack of hæmoglobinuria has been brought on to-day by the cold train journey to London.

Dr. M. Gatman showed on the micro-projector the clumping of the red corpuscles, and the ease with which they are broken up by slight injury such as tapping the microscope slide. The red cells embedded in the adsorbed protein complex are readily ruptured, and their rupture can be observed within the skin capillaries of the patient under the capillary microscope.

Dr. C. H. Whittle: Cases like this may be seen by dermatologists because of the purpura-like lesions. Though not very uncommon the diagnosis may be missed if a blood-count is not made, i.e. if they show no gross anæmia. The condition is to be distinguished from others with Raynaud's syndrome, e.g. acrosclerosis and sclerodactyly, arteriosclerosis, syphilitic arteritis, thrombo-angiitis obliterans and Raynaud's disease, in all of which permanent damage such as atrophy or gangrene is sooner or later found in the extremities (Hunt, 1936). No angiospasm, and no reaction to over-cooling, mark off the clinical condition from the rest of the group. If blood is taken for a count, the diagnosis will be made immediately after a glance at the corpuscles in the counting chamber at room temperature.

REFERENCES

BENIANS, T. H. C., and FEASBY, W. R. (1941) *Lancet* (ii), 479.
BOXWELL, W., and BIGGER, J. W. (1931) *J. Path. Bact.*, 34, 407.
HUNT, JOHN (1936) *Quart. J. Med.*, 5, 399 *et seq.*
MCCOMBS, R. P., and MCELROY, J. S. (1937) *Arch. intern. Med.*, 59, 107.
PARISH, H. J., and MACFARLANE, R. G. (1941) *Lancet* (ii), 477.
ROTH, GRACE (1935) *Proc. Mayo Clin.*, 10, 609.
STATS, D. (1945) *J. Clin. Invest.*, 24, 33–42.
——, and WASSERMAN, L. R. (1943) *Medicine*, 22, 263.

Dr. Parkes Weber: Is there any local pain associated with the attacks?

Dr. Whittle: Tingling and numbness, the usual symptoms associated with Raynaud's phenomenon.

Dr. F. Parkes Weber: I suppose that the degree of pain varies with the degree of the angiospastic part of this "syndrome"—for, of course, it is a syndrome. Extreme pain I have seen only once, and that was in the case of a girl 12 months old (F. Parkes Weber, *Brit. J. Child. Dis.*, 1923, 20, 25). I do not know which of the various types of Raynaud's syndrome has a special right to be termed Raynaud's disease. The Raynaud's syndrome often associated with sclerodactylia I regard as a most important constituent part of the sclerodactylia or acrosclerosis, whichever one likes to call it.

Dr. Whittle: I would refer Dr. Parkes Weber to John Hunt's paper. In his view the most important point about Raynaud's phenomenon is that it is not followed by permanent change in the part. It is a paroxysmal condition which is due to cold, and clears up as soon as the stimulus of cold is removed. On the question of angiospasm, there does not appear to be any here. As far as we know, the picture is made by the clumped red cells in the capillaries of the extremities where the blocking occurs.

Dr. Gatman: Work has been done on this type of Raynaud's syndrome by irrigating the conjunctival sac with ice-cold saline and only agglutinated red cells are to be seen in the small vessels. No angiospasm at all has been seen.

Tropical Lichenoid Dermatitis.—H. J. Wallace, M.D.

G. W., aged 37. This man's dermatitis began in September 1943 three months after his arrival in West Africa. He states that he had no trouble with his skin previously. The skin around the ankles was first affected by a prickly-heat type of eruption. This was followed after a few days by a widespread eruption all over the body, accompanied by marked œdema of the ankles and ulceration of the mouth. Except for a little oozing in the small patches, which became septic, the eruption was dry. The scalp was covered by a crust and shortly afterwards most of the hair fell out. Irritation was minimal but malaise, fever and mental depression marked. After three weeks desquamation began and persisted for months. This was accompanied by areas of pigmentation. Apart from taking mepacrine in suppressive dosage for three months previously, he gave no relevant past history including other drugs or malaria. His diet appears to have been adequate. He continued to take mepacrine for three months after the onset of the dermatitis until he went home.

Recovery to the present state took place slowly over the next few months whilst in England, leaving the sequels which he now shows. In particular, recurrent soreness of the tongue began and has persisted.

He has widespread atrophic areas in the scalp, indistinguishable from pseudopelade. There are gross lichenoid changes in the mouth and tongue and some of the changes are suggestive of early leukoplakia. He has the remains of warty growths on the forehead which have recurred after destruction with cautery. On the whole body there are scattered areas of atrophic lichenoid changes with some scaling.

Comment.—This condition has been widely studied and has been reported from many different parts of the world. There is little doubt that it bears a close, but not fully defined, relation to mepacrine. The clinical features of the patient conform to the normal description of the condition. In particular, however, the leukoplakic changes in the tongue and the widespread atrophy in the scalp are apparently unusual. The continued administration of the mepacrine for three months after the onset of the dermatitis is to be noted.

Dr. R. M. B. MacKenna: I have seen a certain number of these cases, and I consider that the case shown is a true example of the so-called tropical lichen planus. From the military point of view the case belongs to the older age-group of individuals at risk, and it seemed to me that there were mild atrophic changes in the skin of the lower legs; both of these points, which have not been made by previous speakers, are of minor importance but are consistent with the diagnosis.

Dr. Brian Russell: I saw a patient recently who, about nine months previously, had started taking mepacrine, 3·1 grammes in the first week and 0·7 g. in subsequent weeks, but with two periods of 1·7 g. a week interposed. About six months after starting to take the drug he developed lichenized patches, psoriasiform lesions, follicular hyperkeratoses, and a purulent condition of the scalp, with intense itching. The doses recommended for mepacrine are a maximum of 2·8 g. in the first week and

0·7 g. as a maintenance dose in subsequent weeks. This case supported the suggestion that mepacrine eruptions may be the result of high dosage and cumulative action, rather than of idiosyncrasy.

Mycosis Fungoides—Treated with Thorium X.—BERNARD GREEN, M.R.C.S., L.R.C.P.

E. S., male, aged 56. The case was shown at this Section by Dr. Corsi in March 1945 (*Proc. R. Soc. Med.*, **38**, 505).

Duration about thirty-five years. A scaly erythema first commenced on his legs and now is all over the body, including face and scalp. At first it was non-irritating, now it is extremely so. He has a generalized exfoliating erythrodermia with areas of tumefaction, lichenification and many channels of normal-looking skin fairly sharply demarcated. In addition there is loss of hair from the usual areas on the body, together with patches of alopecia on the scalp. There are enlarged lymphatic glands in the inguinal region. The intensity of the rash and the irritation varies, quiescent periods alternating with periods of exacerbation. X-ray treatment had little effect.

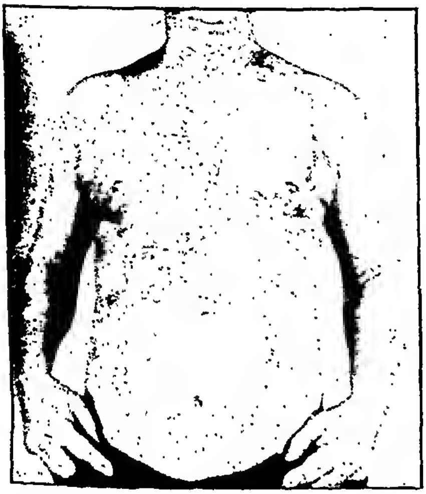


FIG. 1.

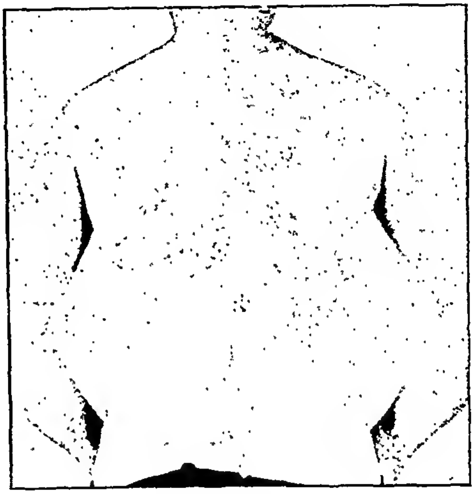


FIG. 2.

Thorium X 2,000 units in iso-propyl alcohol was painted on a small affected area of the skin. This was done once a week six times. This appears to clear the erythema for a time, the effect following the first application; the itching is completely relieved and continues in abeyance, even after some relapse of the erythema. After many weeks without treatment the scaly erythema and the itching return.

It was decided to try a course of intravenous injections of thorium X. 100 units in saline were given once a week twelve times. At first there was some relief of the irritation and some of the erythema diminished. However, I was reluctant to continue with this line of treatment although a differential blood-count taken before, during and after the treatment showed no abnormality.

It was then decided to treat him again with applications of thorium X 2,000 units in iso-propyl alcohol, and this was done once a week twelve times on the whole of the left half of his back and on two square patches on the front of the trunk. The result was again very satisfactory. The erythema and the irritation disappeared and the skin returned to a normal appearance. It is four weeks since the last application and the two squares on the front of the trunk show no return of the erythema (fig. 1) and the itching is completely relieved. On the half of the back painted there is a slight return of the erythema (fig. 2), but the irritation still remains in abeyance.

Mycosis Fungoides.—BERNARD GREEN, M.R.C.S., L.R.C.P.

A. B., female, aged 56. Duration of skin trouble four years. A premycotic eruption of scaly erythema for about one year. Now has in addition multiple tomato-like sessile, rounded, circumscribed tumours all over the trunk, limbs and face. Some of the tumours are ulcerating, causing irritation and discomfort. On the scalp there are areas of cicatricial alopecia with scaly erythema.

Biopsy showed a typical pleomorphic appearance of mycosis fungoides. She has had many X-ray treatments, together with penicillin, T.A.B., &c. X-ray therapy was successful in some degree, some of the tumours treated having disappeared. At other times no results were noted. A course of intravenous injections of thorium X was tried. 100 units in saline were given once a week twelve times. At first the patient reported there was much less irritation for the first few days following each injection, but the appearance of the rash and tumours remained more or less the same. A blood-count done before and after the course of injections showed no abnormality. Nevertheless I was reluctant to continue this form of treatment and thorium X 2,000 units in iso-propyl alcohol was painted on controlled areas of the body once a week twelve times. On the areas painted the exfoliation and the erythema is considerably diminished and the skin has regained a more normal appearance. The irritation remains in abeyance. Some of the tumours were also painted with thorium X in the same strength and these have considerably flattened and become less red. Those which were ulcerating and weeping have dried, become crusted over and diminished in size. On the chin and nasolabial fold, where there was some fissuring, erythema and some loss of the normal elasticity of the skin, considerable improvement has taken place, the fissures having healed and the erythema subsided.

Dr. P. J. Feeny: This is the first time that thorium X has been used parenterally in dermatology, although it has been available since 1912. In the 1920s radio-active thorium injections were used extensively abroad with poor results. In the years just before the late war a case of necrosis of bone after injection of thorium X [1], another case of late bone necrosis seven years after subcutaneous injection [2], a case of radiodermatitis [3], and a case of late radiodermatitis as well as other skin lesions were reported from parenteral use of thorium X [4]. Necrosis of bone both early and late, and radiodermatitis both early and late, have therefore been seen. About two years ago a case of cellular activation and autoradiography was published [5].

Almost all reports have been bad, save in one group, namely, rheumatic conditions [6]. In rheumatism, except gonorrhœal rheumatism [7, 8], the reports have been good. There have been several accidents, however, even with the treatment of rheumatism [9]. At the moment thorium X is being used at the Charterhouse Clinic. Hernaman-Johnson last year published a report on spondylitis favourably treated, and he cited a previous French report [10]. The dose given at the Charterhouse Clinic was 30–100 electrostatic units per c.c. subcutaneously.

We must make up our minds about using thorium X and other radio-active substances internally. I do not think that in dermatology we should start using 100 unit injections of thorium X—it may be found that we should not use it at all internally.

REFERENCES

1 BAZY, L., and COSTE, F. (1938) *Bull. Soc. méd. Hôp. Paris*, **54**, 117.
2 LEFEBVRE, C. (1937) *Mém. Acad. chir.*, **62**, 1446.
3 SÉZARY, A., HOROWITZ, A., LEVY-COBLENTZ, G. (1936) *Bull. Soc. franç. Derm. Syph.*, 43, 601.
4 WEISSENBACH, R. J. (1938) *Bull. Soc. franç. Derm. Syph.*, **45**, 50.
5 MALLET, L. (1944–5) *J. Radiol. Electrol.*, **26**, 4.
6 WEIL, M. P., and GALABERT, R. (1938) *Presse méd.*, **46**, 294.
7 LOUP, P. (1937) *J. Urol. méd. Chir.*, **43**, 238.
8 MARSAN, F. (1937) *J. Urol. méd. Chir.*, **43**, 233.
9 WEISSENBACH, R. J. (1938) *Bull. méd. Paris*, **52**, 35.
10 HERNAMAN-JOHNSON, F. (1946) *Rheumatism*, **3**, 21.

Dr. Green: I quite agree that thorium given intravenously might be dangerous, but in cases of this kind with a grim outlook I felt some justification in trying desperate measures.

Dr. F. F. Hellier: I would like to know if anyone has any experience with nitrogen mustard in mycosis fungoides. This is a new line of attack on certain types of malignant disease. It is a selective method like X-rays, and it affects some cells more than others. The results are only temporary, but it has been useful in certain conditions, and it may have some sort of future in those cases which are resistant to X-rays.

Dr. MacKenna: I have no experience of this particular treatment myself, but reports say that it does relieve the very severe generalized itching which may occur in Hodgkin's disease.

Mycosis Fungoides.—J. R. Owen, M.R.C.P.

M. A., female, aged 61. Cook. 14.10.46: Admitted to hospital, complaining of "lumps on the skin". Condition first noticed in February 1946, following "influenza". At first the lesions very irritable; subsequently less so.

Past history.—Varicose veins nine years ago. Scarlet fever and arthritis, thirty-two years ago. *Family history* not relevant.

Condition on admission.—Good colour and nutrition. C.V.S. Systolic bruit at pulmonary area. B.P. 240/130. Lungs: Diminished breath sounds at left base. C.N.S. normal. Abdomen: Spleen just palpable below costal margin.

Regional lymph nodes not enlarged. Skin: Studded with raised red nodules and irregularly shaped patches of erythema; scaling and superficial ulceration at some points.

X-ray chest: Cardiac shadow enlarged on left with unfolding of aortic arch. Hypertensive heart.

Blood-count (16.10.46): R.B.C. 4,080,000 per c.mm.; Hb 73%; C.I. 0·89; W.B.C. 6,200. Polys. 62·5%, lymphos. 30·5%, monos. 5%, eosinos. 2%. 31.12.46: R.B.C. 4,200,000 per c.mm.; Hb 80%; W.B.C. 3,000. Polys. 64, lymphos. 32, monos. 4%.

Treatment.—Low-voltage therapy. 140 kV. to three small areas (*a*) Right arm 4 cm. field. Max. 2,400 r, min. 1,900 r in twenty-eight days; (*b*) left forearm 4 cm. field. Max. 2,400 r, min. 1,900 r in twenty-eight days; (*c*) left thigh 10 cm. field. Single dose 400 r. 22.10.46 to 25.10.46, daily inclusive: Nitrogen mustard 6 to 7 cc. I.V. 12.11.46 to 15.11.46, daily inclusive: I.V. injections of nitrogen mustard. 1.1.47: Discharged, improved.

Section shows picture characteristic of mycosis fungoides.

Blue Nævus in a Mongolian Patch.—C. L. Collins, M.B.

Mrs. J. M., aged 28, a dairy worker. A dark patch was first noticed on the chest, just below the left clavicle, ten years ago. The area has gradually increased in size and has recently spread upwards on to the left side of the neck. The patient's father came from Barbados, but she does not know of any coloured relation in the family.

On examination.—There is a blue-grey area of skin on the left shoulder and left side of the neck, showing many white striæ. A blue nævus present in the area was removed for biopsy. The rest of the skin is clear.

Report on section.—In the mid-corium there is a zone of very pigmented, ribbon-shaped cells and these can also be seen, though sparsely distributed, in the corium generally.

REFERENCES

Ashmead, A. S. (1905) *J. Cutan. Dis.*, 23, 203; (1934) *Bull. Soc. obst. Gynéc.*, 23, 442.
Cockayne, E. A. (1933) Inherited Abnormalities of the Skin and Its Appendages, p. 69. London.

Dr. F. R. Bettley: This case seems identical with one I recorded in the *British Journal of Dermatology* in 1938, 50, 151. The distribution is the same and it has almost the same linear dimensions to the area. My patient was of about the same age as the patient now presented. The nævus had been present for about fifteen years and was slowly increasing in size. There was the same slaty pigmentation and biopsy gave results which seem to be identical with those given in this case; some of the pigmented cells were Dopa-positive and some negative. I saw my patient again about a year ago, after eight years had elapsed. I had photographs and accurate measurements made, and I found that during the eight years when I had not been observing her there was no increase whatever in the size of the lesions. Apparently they get to a certain size and then stop.

As to the nature of the condition, the only cases I was able to find of the same kind were those described by Darier under the name of melanosis or melanosarcoma. When the term "nævus" is applied to them it is almost begging the question. Treatment presented rather a hopeless prospect. Radium treatment and CO_2 snow made no difference whatever.

Morphœa Guttata.—BRIAN RUSSELL, M.D.

Miss G. G., aged 66. *History.*—1944: Dryness and scaling of skin of the forearms, sacral region, shoulders, and sides of neck. December 1946: A large red patch developed beneath right breast, with intense irritation.

On examination.—A well-nourished woman, of healthy appearance. Mucosæ normal. Skin: Many figurate, slate-coloured plaques with very slightly raised edges, and scaling and atrophy in the centre. Some of the small lesions are polygonal but all show central atrophic changes. These lesions are present under breasts, where they are moist and superficially ulcerated, on front and back of chest and over sacrum, with other smaller lesions near elbows. Supple symmetrical atrophic oval scars above the clavicles. There is an angiomatous papule in a telangiectatic atrophy of vulva.

Biopsy.—Shows hyperkeratosis, with some follicular plugging, thinning of epidermis with absence of rete pegs, and pale, rather structureless collagen in dermis, in which there is slight perivascular round-cell infiltration. The collagen bundles are thickened but pale in the subpapillary region and there is marked disruption of the elastic fibres in this area.

Leucoderma and Leucotrichia.—BRIAN RUSSELL, M.D.

L. W., aged 25. Electrician.

History.—Two to three months: Left eyelashes gradually became white. Two months: Alveolar abscess—tooth extracted under nitrous oxide. One month: Some of left eyebrow hairs became white. *Family history.*—Nothing relevant.

Wassermann and Kahn reactions negative.

On examination (20.11.46).—Apparently healthy man, of placid temperament. Left eyelashes are white. Two small patches of the left eyebrow hairs are white. The skin of the eyelid and orbital region is pale. There is marked acne vulgaris of the back.

? Lupus Vulgaris.—E. COLIN JONES, M.B.

G. W., female, aged 36. Skin trouble began early in 1943 with evanescent reddish areas over the cheeks. In the past she has been variously described as suffering from lupus vulgaris and lupus erythematosus. She had treatment with calciferol 100,000 units daily, with but little benefit.

On examination.—Her condition consists of scattered, indistinctly infiltrated patches on the pre-auricular and cheek areas, the pigmented patch on the right cheek representing the oldest lesion. Although there is a superficial resemblance to erythematoides, the cheek lesions are more those of a lupus vulgaris. W.R. negative. Blood-count normal. No history of drugs. Biopsy suggests a diagnosis of erythematoides.

Dr. Dowling: I would suggest the diagnosis of sarcoid as a possibility in this case—the very superficial type—though with quite perceptible infiltration. The resemblance of that type of sarcoid to lupus disseminatus can be very close.

Favus.—E. COLIN JONES, M.B.

F. T., boy, aged 11. Onset of condition approximately ten years ago while in Egypt. Never previously diagnosed. Scalp is covered by coalescent, dirty, yellowish, adherent crusts, with a typical mousy odour. No typical scutula. The central area shows a somewhat irregular, atrophic, hairless patch. On the body are scars of old patches of favus. Examination of hair shows a typical mycelium, and culture confirms.

Section of Odontology

President—Professor H. Stobie, F.R.C.S., L.D.S.E.

[*January* 27, 1947]

The Sterilization of Dental Handpieces

By Warren Harvey, C. H. LeMay and C. W. Shuttleworth

THE PROBLEM

During the war when one had to inspect hundreds of men and women in about a quarter of the number of minutes, the dish of disinfectant into which the mirrors and probes were dipped was really little but a pretence at sterilization, but I am sure that the personnel would have been more disgusted at its absence than they were at the taste of the fluid. And yet, how often do we sterilize our handpieces? It is not merely the risk of cross-infection but the thought of unhygienic technique which has stimulated this communication.

PREVIOUS METHODS

Hot-air sterilization has been recommended by Parfitt and Herbert (1939) but it is likely from the report of the M.R.C. War Memorandum No. 15 (1945) that a temperature of 160° C. for at least one hour is necessary, with of course special apparatus. Relubrication is then necessary. Autoclaving at 120° C. at 15 to 20 lb. pressure for twenty minutes is recommended by Mead (1940), and by Parfitt and Herbert, but again the apparatus is expensive. Lysol or Bard-Parker solution have been suggested by the same authorities, but there are several disadvantages to these and other chemical methods such as length of time needed (e.g. eighteen hours), corrosion and ineffectiveness, and these have been pointed out in the M.R.C. War Memorandum No. 15 and by Foster, LeMay and Johnstone (1945).

Hot oil has been recommended by Parfitt and Herbert, but has been found unreliable for sterilizing syringes. Oil with a chemical germicide has been suggested more recently by Loretz (1944) and even at 100° C. this is stated to render handpieces sterile after ten minutes; there is a sterilizer on the market with the necessary separate compartment for the oil.

SUGGESTED NEW METHOD

My attention was first concentrated on this problem when during wartime storage conditions, handpieces (which had not been opened since package by the manufacturers) were found to be so corroded that they could not be used. Before the fall of Japan it was necessary to devise a method of storage and lubrication under very unfavourable tropical conditions. After degreasing, all handpieces were soaked in an anticorrosion fluid used by the R.A.F. in gyros; after draining they were sealed in polyvinylchloride envelopes.

Then it was ascertained that a team consisting of an ophthalmic surgeon, a consultant chemist, and a steel technician had overcome the problem of corrosion and is applied to them it is almost begging the question. Treatment presented rather a hopeless prospect. Radium treatment and CO_2 snow made no difference whatever.

Morphœa Guttata.—BRIAN RUSSELL, M.D.

Miss G. G., aged 66. *History.*—1944: Dryness and scaling of skin of the forearms, sacral region, shoulders, and sides of neck. December 1946: A large red patch developed beneath right breast, with intense irritation.

On examination.—A well-nourished woman, of healthy appearance. Mucosæ normal. Skin: Many figurate, slate-coloured plaques with very slightly raised edges, and scaling and atrophy in the centre. Some of the small lesions are polygonal but all show central atrophic changes. These lesions are present under breasts, where they are moist and superficially ulcerated, on front and back of chest and over sacrum, with other smaller lesions near elbows. Supple symmetrical atrophic oval scars above the clavicles. There is an angiomatous papule in a telangiectatic atrophy of vulva.

Biopsy.—Shows hyperkeratosis, with some follicular plugging, thinning of epidermis with absence of rete pegs, and pale, rather structureless collagen in dermis, in which there is slight perivascular round-cell infiltration. The collagen bundles are thickened but pale in the subpapillary region and there is marked disruption of the elastic fibres in this area.

Leucoderma and Leucotrichia.—BRIAN RUSSELL, M.D.

L. W., aged 25. Electrician.

History.—Two to three months: Left eyelashes gradually became white. Two months: Alveolar abscess—tooth extracted under nitrous oxide. One month: Some of left eyebrow hairs became white. *Family history.*—Nothing relevant.

Wassermann and Kahn reactions negative.

On examination (20.11.46).—Apparently healthy man, of placid temperament. Left eyelashes are white. Two small patches of the left eyebrow hairs are white. The skin of the eyelid and orbital region is pale. There is marked acne vulgaris of the back.

? Lupus Vulgaris.—E. COLIN JONES, M.B.

G. W., female, aged 36. Skin trouble began early in 1943 with evanescent reddish areas over the cheeks. In the past she has been variously described as suffering from lupus vulgaris and lupus erythematosus. She had treatment with calciferol 100,000 units daily, with but little benefit.

On examination.—Her condition consists of scattered, indistinctly infiltrated patches on the pre-auricular and cheek areas, the pigmented patch on the right cheek representing the oldest lesion. Although there is a superficial resemblance to erythematoides, the cheek lesions are more those of a lupus vulgaris. W.R. negative. Blood-count normal. No history of drugs. Biopsy suggests a diagnosis of erythematoides.

Dr. Dowling: I would suggest the diagnosis of sarcoid as a possibility in this case—the very superficial type—though with quite perceptible infiltration. The resemblance of that type of sarcoid to lupus disseminatus can be very close.

Favus.—E. COLIN JONES, M.B.

F. T., boy, aged 11. Onset of condition approximately ten years ago while in Egypt. Never previously diagnosed. Scalp is covered by coalescent, dirty, yellowish, adherent crusts, with a typical mousy odour. No typical scutula. The central area shows a somewhat irregular, atrophic, hairless patch. On the body are scars of old patches of favus. Examination of hair shows a typical mycelium, and culture confirms.

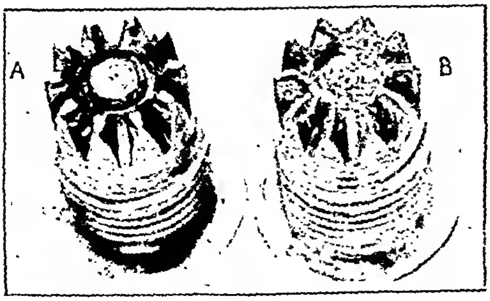


FIG. 2.—The gear from a right-angled handpiece A, lubricated with AC. 10 (Surgical) and boiled in AC. 10 soda is unaffected, whereas gear B from a handpiece lubricated with "dental engine oil" and boiled in water is heavily rusted.

(*b*) *Sterilization.*—Four handpieces, two right-angled and two straight, were sterilized in the usual manner in the hot-air oven. Each handpiece was then immersed in a large tube filled with nutrient broth. The handpieces were completely covered with fluid. The broth was inoculated with *Strep. hæmolyticus* (Group C) and the tubes incubated for twenty-four hours.

The infected handpieces were then transferred to a bath of boiling AC. 10 soda solution for five minutes. They were then taken out and dipped into sterile distilled water and immediately placed in tubes of nutrient broth and incubated for seventy-two hours.

TABLE I.—TEST INCUBATION AFTER FIVE MINUTES IN AC. 10 SOLUTION

	24 hours	48 hours	72 hours at 37°C.
Right-angled handpiece 1 ..	—	—	—
Right-angled handpiece 2 ..	—	—	—
Straight handpiece 1 ..	—	—	—
Straight handpiece 2 ..	—	—	—

The above experiment was repeated, this time boiling in the AC. 10 was continued for ten minutes, with similar results.

Repeat experiments were performed using a highly resistant sporing organism as the infecting agent. Three experiments were performed, boiling the handpieces in the AC. 10 soda solution for ten, twenty and thirty minutes respectively.

TABLE II

Results	10 *min. in AC.* 10 *sol.*			20 *min. in AC.* 10 *sol.*			30 *min. in AC.* 10 *sol.*		
Hours at 37° C.	24	48	72	24	48	72	24	48	72
Right-angled handpiece 1	+	+	+	—	+	+	—	—	+
Right-angled handpiece 2	—	—	+	—	+	+	—	—	—
Straight handpiece 1	+	+	+	—	—	+	—	—	—
Straight handpiece 2	—	+	+	—	—	—	—	—	—

N.B.—The organism used to infect the handpieces in the above series of experiments was *B. subtilis.*

From these results it will be seen that five minutes' boiling of the infected handpieces in the experimental solution rendered them free from organisms as shown by the test incubations. It would appear that this time is sufficient for the destruction of the ordinary non-resistant type of organism infecting dental handpieces.

Ten minutes' boiling failed to sterilize any of the handpieces. Only one was free from infection after twenty minutes' boiling and even after thirty minutes one handpiece gave a growth of infecting organisms after seventy-two hours' test incubation.

From these tests it appears that in order to be absolutely certain of complete destruction of all forms of bacteria it is necessary to boil dental handpieces for over thirty minutes in AC. 10 soda solution. Although it has been reported by Garrod and in the *Brit. Med. J.*, 1941, that five minutes' boiling in 2% sodium carbonate solution kills all organisms including spores, yet it would appear that for instruments the larger subsequent blunting of fine cataract knives by adding sodium carbonate and a fluid known as "AC. 10 (Surgical)" to the sterilizer. It was therefore most gratifying to find that there was a connexion between AC. 10 (Surgical) and the R.A.F. fluid we used to protect our handpieces (Foster *et al.*, 1945).

Exhaustive *ad hoc* experiments, previously reported to the Section of Ophthalmology of this Society (Foster *et al.*, 1945, and Kayser and Foster, 1946), proved that addition of 1% to 2% v/v of AC. 10 (Surgical) to the alkaline aqueous sterilizing solution provided complete protection against corrosion without interfering with sterilizing efficiency (if anything, it helped) and that it was biologically inert and without effect on the metabolic processes of healing. AC. 10 (Surgical) differs from the original AC. 10 only in that it has been modified to obviate "oily" odour when boiling in the sterilizer. It consists of 95% of a light petroleum neutral oil (containing, approximately, 64% paraffins, 31% naphthenes, 5% aromatics) and 5% of a complex of metallic petroleum sulphonates of molecular weights between 400 and 500 and average composition of the order $C_{24}H_{37}SO_3X$—$C_{30}H_{50}SO_3X$.

As this work had demonstrated a means, without alteration to existing equipment, of positively preventing corrosion during, and subsequent to, such a simple and completely effective (Garrod, 1941, &c.) method of sterilization as boiling in 2% soda solution, and as moreover the remnant film was of an oily nature promising lubricant value, it was decided to apply this technique to dental handpieces.

EXPERIMENTAL JUSTIFICATION

(*a*) *Corrosion.*—Two new straight and two new right-angled handpieces were degreased in benzene and dried in an oven. One pair of handpieces was soaked in the AC. 10 (Surgical) fluid for fifteen minutes, while the control pair was soaked in a proprietary dental engine oil; the test handpieces were then put in a sterilizer containing a solution of 2% w/v of crystalline sodium carbonate (decahydrate) and 2% v/v of AC. 10 (Surgical) fluid in water; the control handpieces were then placed in a sterilizer containing water only. All handpieces were boiled for an hour and then dried in an oven at 51° C. overnight. Rust was found on the gears of the right-angled handpiece. The sequence was repeated three more times and then photographs were taken. Figs. 1 and 2 show corrosion of the handpieces (B) which were the controls.

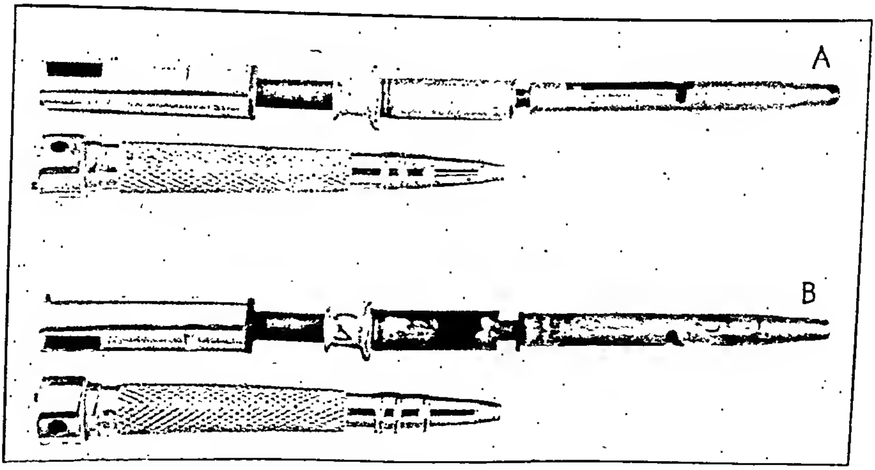


FIG. 1.—Handpiece A, lubricated with AC. 10 (Surgical) fluid, and boiled in AC. 10 soda solution is quite clean; handpiece B, lubricated with a proprietary dental engine oil, and boiled in water, shows considerable corrosion. New handpieces were used.

REFERENCES

EDITORIAL (1941) *Brit. Med. J.*, (i), 894.
FOSTER, J., LEMAY, C. H., and JOHNSTONE, K. I. (1945) The Corrosion of Sharp-edged Ophthalmic Instruments, *Proc. R. Soc. Med.*, 38, 465.
GARROD, L. P. (1941, 1942, 1944) Personal Communication.
KAYSER, J. F., and FOSTER, JOHN (1946) *Proc. R. Soc. Med.*, 39, 835.
LORETZ, M. M. (1944) A Simple Method of Sterilizing, Cleaning and Lubricating Handpieces *Brit. Dent. J.*, 76, 40.
MEAD, S. V. (1940) Oral Surgery. London.
PARFITT, J. B., and HERBERT, W. E. (1939) Operative Dental Surgery. London.
SPEAKMAN, Professor (1946) University of Leeds, Personal Communication.
Med. Res. Counc. (1945) The Sterilization, Use and Care of Syringes, War Memo. No. 15. London.

[*February* 24, 1947]

The "Three-Ply" Structure in Facial Bones

By W. WARWICK JAMES, O.B.E., F.R.C.S., M.Ch.

When war was declared in 1914 no preparation for the special treatment of injuries of the jaws and face had been made. Gradually a definite scheme was evolved and later this was formulated in a War Office Report (1935) leading to the present development of Maxillo-Facial Centres.

The treatment of mandibular lesions was our chief concern at first but those of the upper part of the face became more important and increasingly so with the development of aeroplanes and the increased speed of motor traffic. To-day these injuries have become still more significant and extend to civil life.

My communication is concerned with some features influencing these injuries. Emphasis cannot be made too often upon the great difference between the structure of the dense movable mandible and that part of the face which is fixed to the cranium and provides a base upon which the mandible acts.

The contrast between the dense bone and the thin laminæ of the upper part of the face is particularly noticeable in the macerated skull. The strength of the dense bones is obvious. The thin bones with the mucous membrane attached, possess elasticity as well as strength, whilst lightness is also attained. They provide a powerfully resisting structure.

These characteristics are well demonstrated by anatomical studies and by the experimental investigations carried out by Le Fort (1901) on the cadaver. These studies together with the experience gained from the treatment of jaw injuries showed that the strength and elasticity of thin bones, particularly when supported on either side by the mucoperiosteum with its penetrating fibres, is truly remarkable. Mr. Fickling and I compared their flexibility and strength with three-ply preparations of wood (James and Fickling, 1940, 1941, *a*, *b*).

The force of mastication upon the post-canine teeth of the maxilla is directed through the compact bones of the zygoma of the wall of the orbit to the frontal. Anteriorly the resistance is through the premaxillæ and maxillæ whilst considerable strength is added by the arrangement of the delicate laminæ of bone underlying them. The dense structure of the external surface, on account of the curvature, is not readily recognized in sections.

My own experience led me to think we had more knowledge of details than of a co-ordinated anatomical picture, and that an examination of serial sections through the face would provide a beginning for further study.

I have been greatly helped by Dr. Smout at Birmingham and Professor Lockhart at Aberdeen who have obtained photographs of sections for me. The actual specimens may be seen in the museums of Birmingham or Aberdeen. In addition to these, illusthe mass of metal and the greater the complexity of internal mechanisms, the longer would be the time needed for sterilization.

When necessary AC. 10 (Surgical) fluid can be sterilized by autoclaving as for liquid paraffin.

(*c*) *Lubrication.*—A comparison is shown in Table III of some of the properties of some proprietary dental engine oils and AC. 10 (Surgical).

TABLE III

Oils	A	B	C	D	AC. 10 (Surgical)
Sp. Gr. at 60° F.	0·882	0·882	0·846	0·862	0·879
Fl. Pt (P.M.) Cl. .. °F.	405	430	375	315	310
Visc. R.I. at 70° F. .. secs.	724	919	140	122	120
Visc. R.I. at 140° F. .. secs.	102	119	48	45	43
Visc. R.I. at 200 ° F. .. secs.	49	52	37	35	33

So far as one can judge from criteria of this sort, it is likely that AC. 10 (Surgical) is equally efficient as a lubricant.

(*d*) *Side effects.*—Animal experiments have shown that AC. 10 (Surgical) is biologically inert; remnant traces from sterilization neither have irritant effect nor interfere with metabolic processes.

Silk, glass and natural rubber are not significantly affected (Speakman, 1946), whereas ivory, insulating varnish and synthetic rubber are unaffected.

It is to be expected that the AC. 10 soda solution is, if anything, beneficial to local anæsthetic solutions; for example, when a syringe is boiled in the solution and stored in Smith's solution,[1] drained and filled with Waites Cobefrin local anæsthetic solution the change of pH is as follows:

TABLE IV

AC. 10 (Surgical) soda →	Smith's solution[1] →	Waites Cobefrin in syringe	← Waites Cobefrin in container
pH 9·0-10·0	6·8-7·2	4·6-5·2	2·8-3·6

Thus an alkalizing effect is produced. Professor Berry of the College of the Pharmaceutical Society has concurred in the view that the slight residual alkalinity is likely to be an advantage as far as local anæsthetics are concerned.

I have used this method of sterilizing my handpieces for the last year. The method is very cheap, needing no special apparatus. My sterilizer is emptied and cleaned only once a month and a tenth of a pint of the fluid and six teaspoonfuls of sodium carbonate are added. When evaporation takes place the solution is made up with water only. I soak all the handpieces in neat AC. 10 (Surgical), boil and allow to drain overnight, and boil each after use in AC. 10 soda solution. As with all instruments they are dried in a clean linen towel so that the oiliness is no worry. When cold the AC. 10 fluid separates but re-forms an emulsion on boiling. Occasionally handpieces appear to squeak after several boilings and this is overcome by soaking in neat AC. 10 (Surgical) for a few minutes and reboiling. Local anæsthetic solutions are certainly unimpaired.

Finally, I can keep surgical burrs, reamers, needles and scalpel blades *continuously* in a burr-tray in my sterilizer completely free from corrosion.

I would like to pay tribute to Air Commodore Ballantyne, Director of Dental Services of the R.A.F., who originally gave permission for this work to be carried out, and to thank the Metallurgical Division of the Royal Aircraft Establishment for the photographs.

[1] Phenol 40, sodium biborate 5, glycerin 200, peppermint water 30, distilled water ad 1,500.

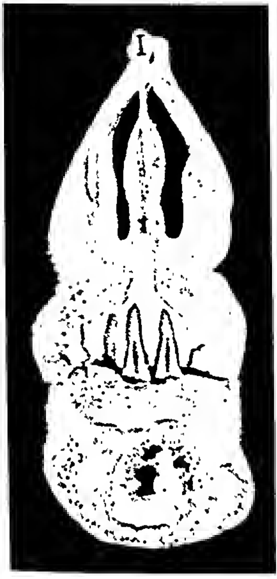


FIG. 1.

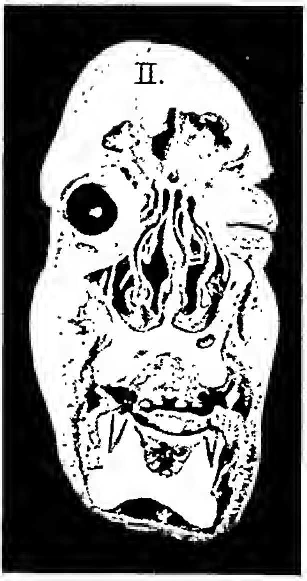


FIG. 2.

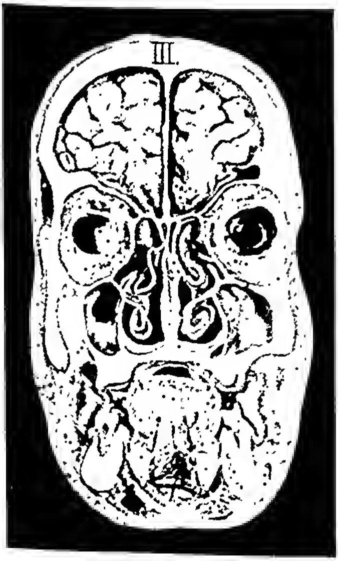


FIG. 3.

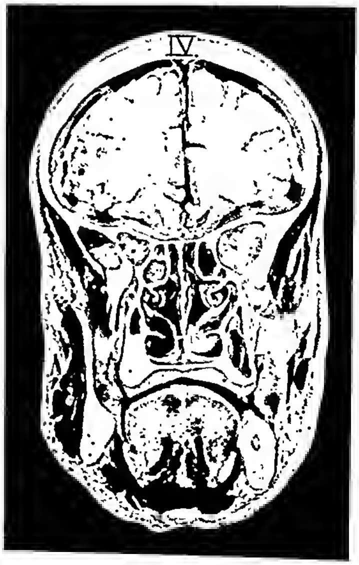


FIG. 4.

(For legends *see* text, p. 512.)

W. WARWICK JAMES: The "Three-Ply" Structure in Facial Bones.

trations were shown from a paper by Professor Reid (1904); tracings modified by Mr. Fickling and me from Eycleshymer and Shoemaker (1911) and an illustration of a disarticulated skull from Schaeffer (1920).

Some explanation is needed of the specially prepared photographs by Dr. Smout. I quote his own words. "I got my artist to photopaque the bones and you may take it that these are accurate and have been most carefully drawn from the specimens. The specimens, from which the photographs were taken, were obtained from a frozen subject which was cut in coronal planes at ½ in. intervals, and mounted in jars; they were not removed but were photopaqued as they stood. The outline of the specimen on the negative was carefully cut out, and retained as a separate entity. Then the areas of bone and cartilage in the negative were blocked out with photopaque, and this prepared negative was printed on gaslight paper which gave a final print with a jet-black background—the bones and cartilage therefore appeared white. The subject was a man unlikely to have been under 60 years of age."

The sections are transverse and vertical, i.e. parallel to the coronal plane. The two sides are not exactly the same on account of the obliquity of cut; this is not intentional, but to maintain an absolute plane is difficult, and moreover not a disadvantage for it shows slight differences.

This communication is an introduction to a subject which needs considerable extension and may suggest a useful line of investigation.

Six of the photopaqued photographs are reproduced here (figs. 1 to 6).

FIG. 1.—Cut through the premaxilla at about the widest diameter of the central incisors. The narrow projection above is due to the incisor crest which is surprisingly high. As the teeth slope slightly upwards and inwards the plane passes through the septum of the nose up to the base of the nasal bones. The Λ-shaped arch, with a limb on either side, is through the nasal bones and the frontal processes of the maxillæ. The fragment of the mandible is cut through the chin.

FIG. 2.—On the left side of the subject the eyelids are present, on the right side the plane passes through the eyeball, being behind that of the left side. This obliquity is indicated by a variation in the position in which the bones of the nose are cut. The thin nature of these bones is obvious. Particularly noticeable is the thin inner wall of the orbit on the left side passing to the inferior turbinal which is also seen on the right side, where external to it, the inner wall of the antrum is distinct. The density of the maxillary and premaxillary bones is obvious and on the left side of the subject a thick plate passes up to the zygomatic bone, cut obliquely. On the right side the zygomatic bone is cut in its posterior aspect where it passes backwards to the zygomatic process. The frontal bone, with large frontal sinuses, is dense above and thin over the orbit below, also dense where it passes to the outer side of the orbit on the right. The character of the mandible is clearly shown.

FIG. 3.—Cut obliquely through the eye on the left side of the subject in front of the outer margin of the orbit accounting for the gap, and with the plane on the right side more towards the back of the orbit. The sections of the thin bones of the nose and inner walls of the orbit and of the antra are distinct. The arch of the frontal bone is dense and below on the outer side of the right orbit is continuous with that of the zygomatic bone. The tongue of bone below this is through the ramus of the mandible. The thicker part of the outer walls of the maxillary sinus is evident on the left side of the subject. Sections through the body of the mandible are seen below.

FIG. 4.—Is through the post-orbital region further forward on the subject's left than right. The back part of the nasal fossæ is well shown. The section cuts the posterior part of each maxilla, exposing the back part of the antrum. The ramus is continuous with the body of the mandible seen on the right; on the left side they are not connected. Inferior orbital fissure is cut across on the left side.

Figs. 5 and 6, *see* p. 514.

REFERENCES

EYCLESHYMER, A. C., and SHOEMAKER, D. M. (1911) Cross Section Anatomy. New York.

JAMES, W. WARWICK, and FICKLING, B. W. (1940) Injuries of the Jaws and Face. London.

——, —— (1941*a*) Experimental Studies upon Fractures of the Upper Part of the Face (Le Fort Translation), *Brit. Dent. J.*, 71, 1, 85.

——, —— (1941*b*) "The Structure of the Bones of the Face in Relationship to Fracture and other Aspects of Facial Injuries", *Proc. Roy. Soc. Med.*, 34, 205.

LE FORT, R. (1901) "Etude expérimentale sur les fractures de la mâchoire supérieure", *Rev. Chir.*, Paris, 23, 208, 360, 479.

REID, R. W. (1904) "Sagittal and Coronal Sections of the Human Head", *Proc. Anat. & Anthrop. Soc.*, Aberdeen, 99.

(1935) Report to the Army Council of the Army Advisory Standing Committee on Maxillo-Facial Injuries.

SCHAEFFER, J. P. (1920) The Nose, Paranasal Sinuses, Nasolacrimal Passageways and Olfactory Organ in Man. Philadelphia.

Section of Laryngology

President—NORMAN PATTERSON, F.R.C.S.

[*February* 7, 1947]

sic Cancer of the Larynx. Review of a Series of Cases

By V. E. NEGUS, M.S.

of the larynx is of sufficient interest to warrant a detailed study, for two There are not only a considerable number of victims of this disease, but also number of these there can be offered a good prospect of cure. Although less frequency than cancer of the stomach and uterus, yet affected cases are r position as regards the eradication of their disease.

e frequency.—As to relative numbers of cases as seen by a laryngologist, I e personally those observed over a period of twenty years (Table I).

ometimes said that intrinsic is more common than extrinsic cancer, but in rds the figures do not support this (Table II).

TABLE I

	Cases		*Cases*
ynx	16	Posterior Pharyngeal Wall	3
Sinuses	51	Larynx (intrinsic)	93
d Fauces	10	Aryepiglottic Fold	17
nd Cheeks	3	Sinus Pyriformis	48
.. ..	19	Post Cricoid	39
. and Epiglottis	15	Œsophagus	188
Total	502		

TABLE II

		Cases
Intrinsic Cancer		93
Extrinsic Cancer		94
Epiglottis	10	
Aryepiglottic Fold	18	
Sinus Pyriformis (with involvement of larynx) ..	37	
Post Cricoid	29	

reparing this communication it has seemed best to me to report all cases of a and not to select a few subjected to one particular form of treatment. It is so to hear of the 75% or 80% of patients cured of cordal cancer; but these ent only a minority, and such a report gives no indication as to the fate of mainder. Accordingly I have made no selection, but give details of every t in this consecutive series.

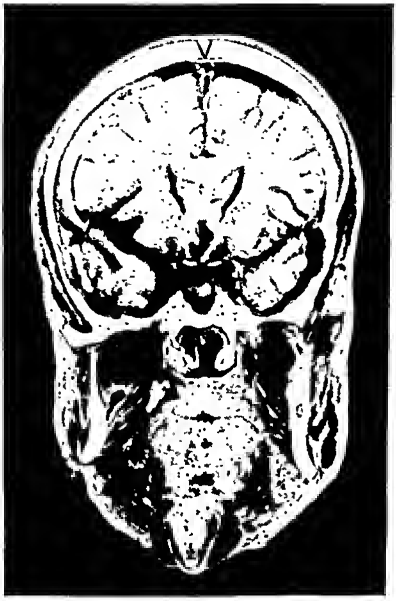


FIG. 5.—The mandible, the only facial bone present, is cut through the rami; that on the left side of the subject is in front of the right as it includes the sub-alveolar canal. The side which is deeper is partly through the coronoid process. The shorter fragment shows the thickening at the back part of the mandible. Eversion of the lower border of the mandible is seen on both. On the left side the attachment of the fibres of the masseter muscle and on the right those of the internal pterygoid are obvious. On the right of the subject, the base of the zygomatic process projects and the bone inside consists of the articular process continued through the wing to the body of the sphenoid.

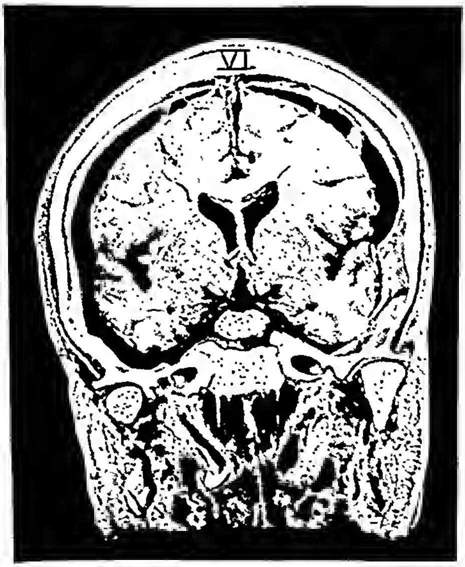


FIG. 6.—The section passes through the temporomandibular joint showing the head of the condyle with a portion of the neck on the left side. The outward projections are through the base of the respective zygomatic processes of the squamous part of the temporal bone. The upper part of the articular fossa is crescentic. The wall of the cranial cavity is seen above, it encloses the brain with the horns of the lateral ventricles centrally situated. On the inside of the joint the end of the petrous portion of the temporal bone and beyond this the basioccipital, are cut across.

The condyles of the mandible are the most posteriorly situated of any of the facial bones.

of disease after five years, and as *promising* if alive and free after a period less than five years, or if dying before the end of five years from other causes, but still free of laryngeal carcinoma.

TABLE IX.—UNILATERAL CORDAL CANCER (35 PATIENTS TREATED)

Results	Cases	Limited 14 C.	P.	F.	Extended 7 C.	P.	F.	Whole cord 14 C.	P.	F.
Laryngofissure	19	3	5	5	2	1	2	–	–	1
Interstitial radium ..	6	1	–	–	–	–	–	1	–	4
Deep X-rays	7	–	–	–	–	–	1	2	3	1
Radium beam	3	–	–	–	1	–	–	–	2	–
	35	4	5	5	3	1	3	3	5	6

Cured 10. Promising 11. Failed 14.

It will be noted that laryngofissure was employed for the limited growths and irradiation for those extending on to the arytenoid.

TABLE X.—UNILATERAL SUBGLOTTIC (5 PATIENTS TREATED)

	Cases	Cured	Promising	Failed
Laryngofissure	1	–	–	1
Interstitial radium ..	3	1	1	1
Radium beam	1	–	–	1
	5	1	1	3

The results, as far as they go, are poor.

TABLE XI.—UNILATERAL CORDAL AND SUPRAGLOTTIC (5 PATIENTS TREATED)

	Cases	Cured	Promising	Failed
Laryngectomy	2	–	2	–
Deep X-rays	2	–	–	2
Radium beam	1	1	–	–
	5	1	2	2

The small number of cases is insufficient to provide conclusive results.

TABLE XII.—BILATERAL CANCER (32 PATIENTS TREATED)

		Limited			Diffuse		
Results	Cases	Cured	Promising	Failed	Cured	Promising	Failed
Laryngofissure ..	3	2	–	1	–	–	–
Laryngectomy ..	20	–	–	–	4	5	11
Deep X-rays	9	1	1	2	–	1	4
	32	3	1	3	4	6	15

Cured 7. Promising 7. Failed 18.

In comparing results, more than one factor must be taken into consideration. In my earlier cases there was less accurate discrimination as to the most suitable treatment, and in the war years of 1939 to 1946 there was much to do in connexion with battle and air-raid casualties, and the sick personnel of the forces; this, together with shortage of nursing staff, meant that operations were avoided as far as possible. Radiotherapy was therefore recommended for some cases who might, otherwise, have been subjected to surgery; the advantage was gained, however, of obtaining a somewhat balanced review of the possibilities available.

To compare the results according to the situation and distribution of the growth, the results in each primary group may be tabulated together, irrespective of the mode of treatment.

Relative merits of various methods.—It is not only the immediate danger to life that must be considered in giving advice, but also the discomforts to be expected during the after-treatment.

(1) *Laryngofissure with removal of one cord or part of both:* The patient does not suffer pain; he swallows a few hours after operation, is out of bed in three or four days and usually leaves after a total stay of two to three weeks. His voice is hoarse but serviceable for all conversational purposes; apart from this there is no disability.

If recurrence appears, further treatment is practicable.

(2) *Laryngectomy:* There is practically no pain after the operation, and if a suction pump be effectively employed, cough is not disturbing. The use of the Sorensen flap and of sulphonamide and penicillin powder in the wound or systemically should guarantee early healing in most cases, usually in less than two weeks. Normal swallowing is then resumed, but œsophageal speech must be learnt. For some patients, especially those of advanced years, this may be difficult or impossible; such patients are then cut off from conversation and may become severely depressed, even so far as to commit suicide. This has happened with two of my cases.

(3) *Interstitial radium:* An operation is required and sepsis may supervene. The needles must cover the subglottic region, and part of the cricoid should be removed. Perichondritis or stenosis are possible sequelæ. If successful, the method may restore the voice almost to normal. If recurrence occurs, laryngectomy is possible, and has been performed twice by me with no undue difficulty. The treatment is short and no tracheostomy is required.

(4) *Deep X-ray therapy:* The treatment is tedious, and must be prolonged over four or five weeks; it produces a feeling of ill-health, often with excessive secretion. Perichondritis may ensue, or may follow even after a lapse of years. The growth may be arrested but not cured, and slow spread may kill the patient after a prolonged period of suffering, greater in severity and duration than if no such attempt at cure had been made. In my opinion, the mere prolongation of life is no criterion of success.

If successful, the larynx may be restored to normal appearance, with a clear and resonant voice.

(5) *Radium beam:* The same disadvantages may arise, but usually in lesser degree; the local discomfort to the patient appears less than with deep X-ray therapy, but treatment is more tedious.

Perichondritis after irradiation: This danger is a real one, as these figures show:

TABLE VIII

	Cases treated	Perichondritis	Recovered	Died
Interstitial radium ..	9	2	1	1
Deep X-rays ..	24	4	2	2
Radium beam ..	10	2	0	2
	43	8	3	5

The affection of cartilages and of the soft tissues overlying may be of low grade and prolonged; treatment in the past appeared ineffective, but penicillin may prove effectual in some cases. In the insertion of radium excessive dosage may have been at fault in the patient who died.

Results of treatment according to situation of growth.—It is difficult to fix a criterion of success. A three-year period of freedom is useless, since I have seen late recurrences after laryngofissure, when operation had been performed according to the tenets of StClair Thomson, with wide removal of the endolarynx. Thus 2 patients, at first apparently free of disease, had recurrences after three years, and 1 other after four years; these are naturally not classed here as successes, thus detracting from the percentage of cures. I have classed patients as *cured* only if they were well and free

The treatments by irradiation were under the direction of experts, with efficient equipment. Irradiation seems to be ineffective in recurrent cases.

TABLE XVI.—COMPARISON OF METHODS OF TREATMENT

		Cases	Cured	Promising	Failed
Laryngofissure	primary	23	7	6	10
	secondary	1	–	–	(1)
Laryngectomy	primary	22	4	8	10
	secondary	4	1	(1)	(2)
Interstitial radium		9	3	1	5
Radium collar		1	–	–	1
Deep X-ray	primary	17	4	5	8
	secondary	7	–	–	(7)
Radium beam	primary	5	3	1	1
	secondary	5	–	1	(4)
		79+(15)	22	22+(1)	35+(14)

(The figures in brackets refer to patients already included)

It is impossible, in any analysis, to make an exact comparison of alternative methods, since that is adopted which appears most likely to benefit the various groups of patient. The situation, distribution and type of growth, the general condition of the patient, the skill of the surgeon or radiotherapist, and the environment of treatment are all factors which must be considered.

I believe that my present percentage of cures by laryngofissure would compare favourably with those published by others; I have had many disappointments from laryngectomy, but not, I venture to believe, from errors of technique.

Choice of treatment.—For me, the experience of these cases, spread over a period of twenty years, has allowed certain conclusions to be drawn.

(1) A growth limited to the membranous vocal cord is best treated by removal through the *laryngofissure* route. The figures given may not appear startling, but at the present day I should feel able, after selecting the case with all due care, to promise the patient a very good prospect of permanent cure, with little danger to life, with but slight suffering and with no subsequent disability except a somewhat husky voice.

(2) A unilateral cordal growth extending on to the arytenoid cartilage, or reaching the posterior commissure, and without fixation, would be treated by *external irradiation*. The alternative would be interstitial radium, but the former appears to offer a more even irradiation, although with more prolonged discomfort to the patient. Surgical treatment, if carried out, would entail removal of the whole larynx, with the loss of the natural voice and with no guarantee against recurrence.

(3) A diffuse growth arising in the larynx affected by chronic hypertrophic laryngitis, an extensive subglottic carcinoma or a growth widespread and with marked fixation of the cord, would be treated by *total laryngectomy*.

(4) Cases of recurrence after laryngofissure are best treated by *total laryngectomy* if otherwise suitable. External irradiation for recurrent cases has not given sufficient success to be justified.

CONCLUSIONS

Of patients presenting themselves with malignant disease of the larynx, of various types and at different stages of progress, 22 were permanently cured and 22 others were free of disease but had not passed the five-year standard; in 35 cases treatment failed, although the disease was in some instances arrested for some years. The intervention of the war years disturbed the keeping of records and in some cases adversely affected the treatment of patients.

I wish to acknowledge the help of my colleagues at King's College and Horton Emergency Hospitals, and also the radiotherapists who have treated patients referred by me; among them are Drs. Finzi, Langmuir Watt, Levitt, Allchin, Dr. Wood of the Radium Beam Therapy Research, and Professor Windeyer. From the latter,

TABLE XIII

	Cases	Cured	Promising	Failed
Unilateral cordal cancer..	35	10	11	14
Unilateral subglottic ..	5	1	1	3
Unilateral cordal and supraglottic	5	1	2	2
Bilateral cancer	32	7	7	18
	77	19	21	37

The results, both of those known to be free of disease after five years, and also those promising to be cured, are less good in the bilateral and subglottic groups, as might be expected. But the figures are not so divergent as might be looked for; the difference is better reflected by the severity of treatment required for more extensive growths.

Metastases and recurrences.—In only 4 of the series were palpable glands present before the commencement of treatment; the patients were not refused for this reason. In 8 cases enlarged cervical glands appeared after treatment; 5 were treated by block dissection and 3 by irradiation. One patient was noticeable as having a further recurrence after an apparently complete surgical removal; he responded to irradiation and it might therefore be presumed that this treatment would have been effective in the first place. General opinion favours the view however that for differentiated growths surgical removal of secondary glands is the correct procedure.

TABLE XIV

		Site of recurrence after temporary freedom from disease				
Primary treatment	No. of pts. with recurrence	Cervical glands	Larynx	Laryngectomy scar	Trachea	Mediastinum
Laryngofissure	7	–	5	–	2	–
Laryngectomy	8	5	–	2	5	1
Interstitial radium ..	1	–	1	–	–	–
Deep X-rays	3	3	–	–	–	–
Radium beam	1	–	1	–	–	–
	20	8	7	2	7	1

The possibility of recurrence indicates the necessity for careful selection of the right treatment, for wide endolaryngeal excision, for avoidance of narrow field laryngectomy and for removal of a sufficient length of the trachea in subglottic cases.

Treatment of recurrences.—Here a difficult problem is presented, since the results have generally been poor in my experience.

TABLE XV

Secondary method of treatment	Cases	Cured	Promising	Failed
Laryngofissure	1	–	–	1
Laryngectomy	4	1	1	2
Deep X-rays	7	–	–	7
Radium beam	5	–	–	5
	17	1	1	15

This presents a gloomy picture and gives the impression that if the primary treatment fails, the prognosis is extremely bad. The patient cured had been treated originally by teleradium; of the remainder, one had a previous laryngofissure on the opposite side and twelve of the others also had laryngofissure. Three were irradiated after laryngectomy, but without success.

As for the reasons for recurrence, I can offer no logical explanation. The operations were carried out with no restriction and a surrounding area of healthy tissue sufficient in extent appeared to be included in every case. Microscopical sections were examined to decide whether any growth had been left; in one doubtful case after laryngofissure, the larynx was reopened a week later and the posterior area coagulated by diathermy.

The subglottic cases had not been so satisfactory as the others; the unilateral supraglottic cases were more satisfactory, but not very good:

Treated by	Unilateral subglottic 5				Unilateral supraglottic 16			
	T.	C.	P.	F.	T.	C.	P.	F.
Limited surgery ..	–	–	–	–	1	–	–	1
External radiation ..	5	1	1	3	15	2	4	9
Total	5	1	1	3	16	2	4	10

Only a very small number of bilateral limited lesions had been treated:

Treated by	Bilateral Limited 6				Advanced 12 (Unilateral or bilateral)			
	T.	C.	P.	F.	T.	C.	P.	F.
External radiation ..	6	3	1	2	11	2	1	8
Interstitial radium ..	–	–	–	–	1	–	–	1
Total	6	3	1	2	12	2	1	9

The advanced group included cases of unilateral carcinoma in which the growth had invaded the thyroid, and here results and mortality figures were not so good.

The treatment of cases of hypertrophic laryngitis had not been successful except for one case which was treated by total laryngectomy.

HYPERTROPHIC LARYNGITIS	Primary		Secondary Treatment		
Treated by	Total	Failed	Total	Cured	Failed
External radiation ..	3	3	–	–	–
Interstitial radium ..	1	1	–	–	–
Total laryngectomy ..	–	–	3	1	2
Total	4	4	3	1	2

His next table showed the total cases in which radical treatment was attempted:

INTRINSIC CARCINOMA OF LARYNX	Radical treatment 1931-1941				Deep X-rays alone 1942-1943		
	T.	C.	P.	F.	T.	P.	F.
Limited surgery ..	5	2	1	2			
Total laryngectomy							
Primary	1	–	–	1			
Secondary	7	(2)	1	(4)			
External radiation							
Primary	53	17	7	29	20	12	8
Secondary	19	1	(1)	9+(8)			
Interstitial radium ..	2	–	–	2			
Total (Primary)	61	19	8	34	20	12	8

(The figures in brackets refer to patients already included.)

The final results in 81 cases showed 19 cured and 20 promising, making a total of 39, which was very similar to the figure given in the final table which Mr. Negus had shown. The interesting point was that 73 out of these 81 patients were treated by external irradiation whereas in Mr. Negus's series, out of a total of 79, there were 45 who were treated either by laryngofissure or total laryngectomy.

and from Mr. C. P. Wilson, I have derived much information, and many cases have been referred by me for treatment under their care.

Mr. Negus *showed five patients to illustrate the various methods of treatment of cancer of the larynx and the resulting voices.*

The first had a localized carcinoma of one cord, and was treated by excision through the laryngo-fissure route in 1936. He has remained in good health and is able to carry on his work without difficulty, including a good deal of talking to numbers of people.

The second had a carcinoma extending along the whole length of the cord, too extensive for local excision. Radium needles were inserted thirteen years ago and the patient has a good and powerful voice.

The third was seen early in 1942, with an extensive carcinoma involving the whole of one cord and also the subglottic region. He was treated under the care of Mr. C. P. Wilson and Professor Windeyer with deep X-ray therapy. His voice is now perfect and the larynx appears normal.

The fourth patient sought advice in 1938, and was found to have a carcinoma extending to the posterior commissure and also spreading anteriorly to the base of the epiglottis. There was some limitation of movement, but no obvious subglottic extension. He was treated by Professor Windeyer with teleradium and has a perfect voice and a larynx normal in appearance. He has given many lectures during the war.

The last patient was seen in 1938 with a longstanding history of hoarseness and with a note of removal of what appeared to be granulomata seven and two years previously. There was a diffuse carcinoma, with some limitation of movement, and subglottic extension causing dyspnœa. The carcinoma was of Broders' Group II. Laryngectomy was performed, and since this operation the patient has led a normal life and was able to make his voice audible to the large audience at the meeting.

Professor B. W. Windeyer said that he had some figures of his own to present from the Middlesex Hospital which were on a comparable basis to those of Mr. Negus.

His figures related to the total number of cases of intrinsic carcinoma of the larynx received in Middlesex Hospital from 1931 to 1943. Those years were chosen because the period from 1931 to 1941 included the five-year "cures", and the later two years, 1942-1943, brought in some extra cases in which cure had been maintained for at least three years. He had produced his own figures in the same way as Mr. Negus had done and according to the same criteria. Since 1932, when they obtained a 1-gram radium unit, he had, in close co-operation with Mr. C. P. Wilson, set out to record the results obtained by the use of external irradiation. A large bias towards external irradiation would be noticed in his figures, and only a small number of cases had been treated by laryngectomy.

He was grateful to Mr. Wilson for his co-operation in these cases because he knew what a great trial it was to him as a surgeon to see cases which he must have thought suitable for total laryngectomy being handed over for treatment by irradiation.

His first table showed the total number of cases during the years mentioned:

Intrinsic Carcinoma of Larynx

Total No. of Cases 106. Male 102. Female 4

	1931-1941	1942-1943
Radical treatment (primary)	62	24
Incomplete or palliative treatment ..	–	2
Treatment for recurrence	12	–
Untreated	4	2
Total	*78*	*28*

Unilateral Cordal Cancer (38 cases)

		Limited 11				Extended 15				Whole cord 12			
Treated by	Total	T.	C.	P.	F.	T.	C.	P.	F.	T.	C.	P.	F.
Limited surgery ..	4	3	2	1	–	–	–	–	–	1	–	–	1
Total laryngectomy ..	1	–	–	–	–	1	–	–	1	–	–	–	–
External radiation ..	33	8	2	4	2*	14	3	5	6	11	5	2	4
Total	38	11	4	5	2	15	3	5	7	12	5	2	5

*One of these was later cured by total laryngectomy (Alive and well now after eight years)

Section of Anæsthetics

President—STANLEY ROWBOTHAM, M.D.

[*March* 7, 1947]

DISCUSSION ON LOCAL ANALGESIA

Dr. Norman R. James: *Premedication.*—One of the most important aspects of local analgesia is that of premedication. This does not consist merely in the haphazard administration of a hypnotic drug just prior to operation but in a carefully planned course of preoperative treatment designed to ensure that the patient has the maximum mental and physical comfort preceding and during the induction of the local analgesia and the subsequent operation.

The system of premedication which I have eventually found most satisfactory is as follows: Whenever possible the patient is visited the day before operation and the question of local analgesia frankly discussed and the reasons for its use fully explained. The ultimate choice should be left entirely to the patient. If he decides against it, there and then the anæsthetist should agree in an affable manner to administer a general anæsthetic despite his inclinations to the contrary. An exception to this rule is when the choice of local analgesia to the exclusion of general anæsthesia may mean a life-saving measure, such as in an advanced stage of intestinal obstruction.

Even here a tactful explanation during the administration of the local analgesia should be given, providing the patient is in a fit mental state to appreciate it.

The drug best suited to ensure the patient a tranquil night preceding operation without subsequent nausea is luminal (syn. phenobarbitone) which should be given in a dose of 1 to 3 grains by mouth according to the age, physique and condition of the patient. One and a half hours before operation the patient should be given a hypodermic injection of omnopon grain $\frac{1}{6}$ to $\frac{2}{3}$ using a fine sharp needle and not the usual blunted or barbed variety so commonly found in hospital wards, which tend right from the start to make the patient "needle shy" when local analgesia is to be used.

Presuming that the local analgesia is to be administered by the surgeon, then half an hour before operation the patient should be given, preferably in his bed (if the anæsthetist can spare the time), a *very* slow intravenous injection of 5% nembutal (pentobarbital sodium). After each c.c. has been injected there should be a pause and the patient questioned as to his feelings and asked to close his eyes and then open them quickly. The moment he shows signs of having developed a definite nystagmus together with a thick slurred speech of euphoric tendency similar to that of a person in a pleasant state of light alcoholic intoxication, then the injection is discontinued. If left alone the patient will often relapse in a few minutes into a deep sleep but can be quickly aroused and when awake is fully co-operative. The intravenous injection of nembutal should never be pushed beyond this pleasant stage because he will then tend to go into a state of basal narcosis and non-co-operation. After my five years of

It was difficult to say whether teleradium would produce better results than X-ray therapy. In the first series of cases teleradium was used as first preference. From the table it would be seen that 28 cases were treated, of whom 10 were classed as cured and 4 as promising, making 14 out of 28. During that time 22 cases, generally less favourable ones, were treated by X-rays and the results were not so good—6 cured and 3 promising.

EXTERNAL RADIATION	1931-1941				1942-1943		
	T.	C.	P.	F.	T.	P.	F.
Teleradium							
Primary	28	10	4	14	–	–	–
Secondary	7+(4)	–	–	7+(4)	–	–	–
Deep X-rays							
Primary	22	6	3	13	20	12	8
Secondary	3+(5)	1	(1)	2+(4)	–	–	–
Teleradium and Deep X-rays	3	1	–	2	–	–	–
Total (Primary)	53	17	7	29	20	12	8

In the 1942-43 period, when they were not using teleradium, and all cases were treated by X-rays, the results—none of them of less than three years and some of them approaching the five-year period, but still only classed in the promising group—showed that of 20 cases, 12 were in the promising group. The result with X-rays, adding the whole series together, was just about the same as had previously been obtained with teleradium.

Perichondritis was the bugbear of external irradiation in the treatment of carcinoma of the larynx. In some of the cases a very severe perichondritis had been experienced, and a number had lost their lives as a result of it. Others, as Mr. Negus had stated, had had a "niggling" irritation or pain which had been very distressing. They hoped to be able to control this sequel better by systemic penicillin which was being tried out.

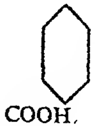
Mr. Negus had raised the question whether the histological classification was of very great importance. He believed that no very definite difference had been found between the undifferentiated and the more differentiated cases.

Finally as to treatment, he thought that their results would have been improved if more total laryngectomies had been done on cases, particularly the advanced ones, which were now thought to be suitable for that procedure and not suitable for irradiation. With regard to the early case which Mr. Negus had said should be treated by laryngofissure, he thought that the results of that treatment and of external irradiation showed no very great difference. The voice of the patient who was irradiated was a better voice than that of the patient on whom laryngofissure had been done, although that also might be quite good. There was no doubt that the patient undergoing external irradiation had a much longer treatment and an unpleasant treatment, partly because of the painful reactions which he experienced and partly because of the prolonged and wearying nature of the treatment itself. For the treatment of an early case his preference would be external irradiation.

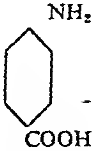
There was one other feature about teleradium and X-ray therapy, namely that the actual course of treatment with X-ray therapy meant shorter sessions for the patient. This was certainly so with the teleradium unit at their disposal—a 4-gram unit—with which each individual session lasted over an hour, whereas with X-ray therapy the individual treatment was not more than perhaps ten minutes.

These two papers, together with the subsequent Discussion, will appear in the *Journal of Laryngology and Otology*.

Dr. Frederick Prescott: *The chemistry and pharmacology of local analgesic drugs.*—With a few exceptions most local analgesic drugs are derivatives of benzoic or para-aminobenzoic acids

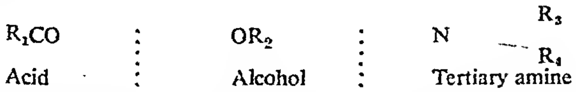


Benzoic acid



Aminobenzoic acid

Their activity depends upon the presence of the structure



$$\underset{\text{Acid}}{R_1CO} \;\vdots\; \underset{\text{Alcohol}}{OR_2} \;\vdots\; \underset{\text{Tertiary amine}}{N\begin{matrix}R_3\\R_4\end{matrix}}$$

in which R_1, R_2, R_3 and R_4 stand for different organic groups or radicals. This is only generally true; actually there are local analgesic drugs with no tertiary amine group in them, e.g. benzocaine, orthocaine and butesin (*see* Table II), while nupercaine is derived neither from benzoic acid nor from para-aminobenzoic acid.

The more common local analgesic drugs derived from benzoic acid are shown in Table I, in which B.A. stands for the benzoic acid grouping. The more common drugs derived from para-aminobenzoic acid are shown in Table II.

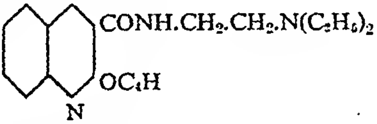
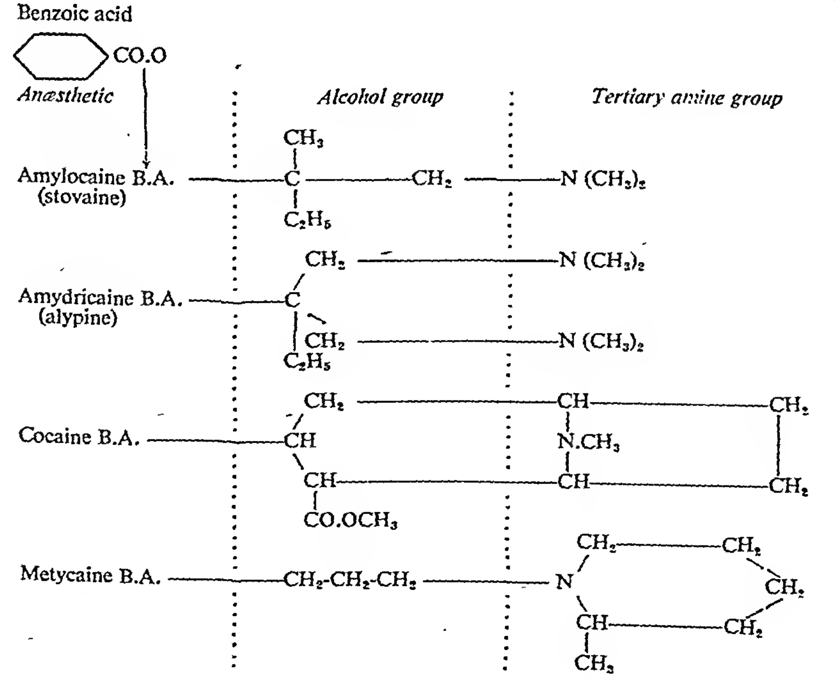
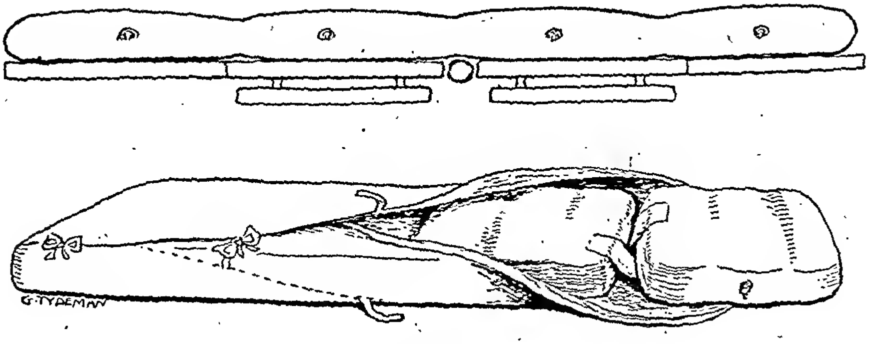
Nupercaine 
CONH.CH₂.CH₂.N(C₂H₅)₂
OC₄H
N
is a derivative of quinoline and contains a tertiary amine group, but no alcohol or benzoic acid or para-aminobenzoic acid groupings.

TABLE I.—LOCAL ANÆSTHETIC AGENTS DERIVED FROM BENZOIC ACID


Benzoic acid
CO.O
Anæsthetic
Alcohol group
Tertiary amine group
Amylocaine B.A. (stovaine)
CH₃
C
CH₂
N (CH₃)₂
C₂H₅
Amydricaine B.A. (alypine)
CH₂
N (CH₃)₂
C
CH₂
N (CH₃)₂
C₂H₅
Cocaine B.A.
CH₂
CH
CH₂
CH
N.CH₃
CH
CH
CH
CH₂
CO.OCH₃
Metycaine B.A.
CH₂-CH₂-CH₂
N
CH₂
CH₂
CH₂
CH
CH₂
CH₃

experience with intravenous nembutal preceding local analgesia for general surgery I have come to the conclusion that it is the only successful method when compared with the unreliable results obtained by giving it or similar barbiturates by mouth or *per rectum*. Recently Dr. R. P. W. Shackleton and I have applied it in the premedication of patients having local analgesia for plastic surgery. These patients, mostly ex-Service men, who have undergone many operations in various hospitals since their initial injury are all connoisseurs of anæsthesia and in most cases insist on the employment of intravenous pentothal. Many have unfortunately experienced the inefficient application of local analgesia at one time or another and are naturally biased against its subsequent employment for a suitable operation. Those willing to give intravenous nembutal premedication followed by local analgesia a trial are generally enthusiastic about it afterwards and are subsequently quite willing and in fact eager to undergo it again. Often there is partial or total amnesia for many hours following the operation and there is usually an uneventful recovery. The only sequelæ recorded have been slight nausea or "hangover" in two cases, one of these patients admitting later that he was a very heavy rum drinker. Needless to say nembutal should not be used when barbiturates are generally contra-indicated such as in hepatic or renal failure. Its use is also contra-indicated in intra-abdominal operations, such as gastrectomies. In these cases intravenous omnopon given in slow fractional doses according to the condition of the patient is the practical choice. Scopolamine is always contra-indicated in a conscious patient owing to the discomfort of a dry mouth with intense thirst which follows its use; and occasionally the patient may develop uncontrolled restlessness and even delirium. It is wrong to deprive the patient of meals prior to non-abdominal operations providing the meal is of a suitable light nature. Lack of nourishment often gives rise to a feeling of discomfort and faintness before and during operation.

In the past (with the exception of Robert Farr) little interest has been taken in the comfort of the operating table on which the patient might have to lie for two hours or more. The ordinary Sorbo covering is practically useless. A Dunlopillo cellular type of rubber mattress is an improvement. I have evolved after several experiments, with the aid of a grant from the M.R.C., a useful form of pneumatic mattress in sections (*see* figs. 1 and 2).



FIGS. 1 and 2.

The various sections for head, chest, lumbar region, &c., can be inflated to any desired tension in order to fit the particular patient's body contours. The inflation is performed by pressing on to the Schraeder nipples supplying each section, a B.E.N. type of automatic air chuck connected by a length of tubing to a small CO_2 cylinder via a reducing valve. The various sections are all bound together by flexible straps and enclosed in a washable canvas cover. Should a section be found to be overinflated and the patient not feel comfortable the pressure can be immediately reduced to comfortable proportions by pressing on the Schraeder valve just as when deflating an automobile tyre. Experience has shown that overinflation is the usual mistake in adjusting such mattresses to the comfort of the patient.

Where possible the patient should always be blindfolded when in the operating theatre by means of a folded piece of lint or similar opaque material and this does not tend to annoy the patient by tickling if it is damped with warm water before application. Conversation in the theatre should be minimal and nothing said or done to undermine the peace of mind and confidence of the patient. The surgeon should always warn the patient before starting to inject the local analgesic solution that he will feel a slight prick of the needle.

All these small points combined with the certain results obtained by the *intravenous* injection of nembutal, in contradistinction to its oral or rectal use, tend to give the maximum success when local analgesia is applied to suitable operations.

which are structurally related to it, replace it in the enzyme system, which, however, is blocked as it cannot utilize the substitute.

Mr. H. W. L. Molesworth: Even with the great advances in inhalation and intravenous anæsthesia, there are still some advantages to the surgeon and to the patient in regional analgesic methods.

One of these advantages is the relatively bloodless field, which has been termed a "physiological tourniquet". This advantage is most apparent in two regions, namely, the breast and the neck, where the technique lends itself to administration by the anæsthetist before the patient comes into the operating theatre.

The advantage of a bloodless field carries with it the obligation on the part of the surgeon to carry out most careful hæmostasis. But vessels which require ligature will bleed sufficiently to show, and I have not yet found that post-operative hæmatomas are more common, or, indeed, so common, as they are with general anæsthesia.

The technique which I use for the induction of analgesia for a major breast operation follows very closely one which was worked out by Mr. C. E. Corlette of Sydney, and I have had uniformly satisfactory results in 25 cases.

The patient must be adequately premedicated, and I have used the method of Mr. Corlette over the last two years in which morphine-sulphate and hyoscine are given in doses, arranged according to the patient's age and sex, at intervals of two hours before operation and one hour before operation, rather than the intravenous technique which Dr. Norman James has described (Table I).

TABLE I.—PREMEDICATION SCHEME, SHOWING DOSES FOR AGE-PERIODS
The dosage stated is founded on experience of pre-war Hyoscine

Age in yrs. (inclusive)	Sex	Time to be given before operation	Doses in grains		Doses in milligrammes	
			Morphine sulphate	Hyoscine-hydrobromide	Morphine sulphate	Hyoscine hydrobromide
14 and 15	Both sexes	two hours	1/4	1/150	16·0	0·4
16 to 19	F.	two hours	1/4	1/100	16·0	0·65
		one hour	1/8	—	8·0	—
16 to 19	M.	two hours	1/4	1/100	16·0	0·65
		one hour	1/6	1/200	11·0	0·3
20 to 29	F.	two hours	1/3	1/100	22·0	0·65
		one hour	1/6	1/150	11·0	0·4
20 to 29	M.(1)	two hours	1/3	1/100	22·0	0·65
		one hour	1/6	1/150	11·0	0·4
		(1)	1/8	1/300	8·0	0·2
30 to 34	F.	two hours	1/3	1/100	22·0	0·65
		one hour	1/6	1/300	11·0	0·2
30 to 34	M.	two hours	1/3	1/100	22·0	0·65
		one hour	1/6	1/150	11·0	0·4
35 to 49	F.	two hours	1/3	1/100	22·0	0·65
		one hour	1/6	—	11·0	—
35 to 49	M.	two hours	1/2	1/100	33·0	0·65
50 to 54	F.	two hours	1/3	1/150	22·0	0·4
50 to 54	M.	two hours	1/3	1/150	22·0	0·4
		one hour	1/6	—	11·0	—
55 to 74	Both sexes	two hours	1/3	1/150	22·0	0·4
75 to 84	Both sexes	two hours	1/4	1/200	16·0	0·3

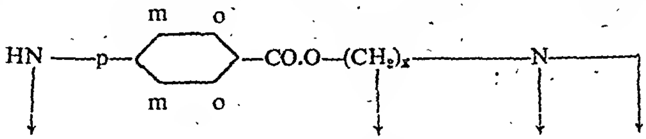
(1) In this group a third intravenous injection of morphia may be needed.

The technique for an operation for carcinoma of the breast involves injections for the induction of analgesia and, in addition, injections whose object is to constrict the main blood-vessels supplying the area to be operated on. The whole procedure has taken, in my hands, from twenty-five to thirty minutes, and where this is done by the surgeon it obviously means that a breast operation will take longer than under inhalation anæsthesia. A certain amount of time is saved in dealing with bleeding points. Where, however, the analgesia is induced by the anæsthetist while the surgeon is scrubbing up or finishing the last case, quite a considerable amount of time is saved.

The patient is wheeled into the anæsthetic room and a brachial plexus block induced by the well-known Kulenkampf technique, using up to 30 c.c. of 2% ethocain in an isotonic solution containing adrenaline hydrochloride 1/250,000. It is of some importance that a 2% ethocain solution requires but 0·55% of sodium chloride to make it isotonic.

TABLE II

LOCAL ANÆSTHETIC AGENTS DERIVED FROM PARA- AND ORTHO-AMINOBENZOIC ACID



Benzocaine (Anæsthesin)	H		C_2H_5 (Ethyl)	None	None
Butesin	H		C_4H_9 (Butyl)	None	None
Orthocaine (Orthoform)	OH	NH_2 in *m*- not *p* position	CH_3 (Methyl)	None	None
Amethocaine (Decicaine)	C_4H_9		$(CH_2)_2$	CH_3	CH_3
Butyn	H		$(CH_2)_3$	C_4H_9	C_4H_9
Larocaine	H		$CH_2:C(CH_3)_3$	C_2H_5	C_2H_5
Monocaine	H		$(CH_2)_2$	C_4H_9	H
Procaine	H		$(CH_2)_2$	C_2H_5	C_2H_5

The local analgesic drugs are weakly basic or alkaline and their salts, which are the compounds employed clinically, are acid in reaction, with a pH of from 4 to 6. It is probable that the free base is liberated in the slightly alkaline tissues. With few exceptions, e.g. amethocaine, nupercaine, and metycaine, solutions of local anæsthetic drugs are destroyed on autoclaving. This is important from the point of view of their sterilization. In the preparation of weak solutions (i.e. 1% or less) distilled water should not be used as the resulting solution is hypotonic. Thus 1% procaine solution will hæmolyse red cells and rupture connective tissue and fat cells. Therefore normal saline should be used for making such solutions. Care should be taken over the glassware used for the storage of solutions as alkali glass causes decomposition. This is because alkali liberates the less stable base from the salts. Actually alkalis potentiate the action of local anæsthetic drugs if added immediately before use as they liberate the free base, which is the compound acting on the nerve endings. In practice it is not advisable to add alkali as the solution becomes turbid and cannot be sterilized by heating. It is stated that solutions of local anæsthetic agents in the strengths normally used are often bactericidal. This is true, but although they may kill pathogenic organisms, spores are not killed nor are some moulds.

The action of local anæsthetic drugs is potentiated not only by adrenaline, but by most of the sympathomimetic vasoconstrictors. This is because their duration of action is proportional to the time they are in contact with nerve tissue and vasoconstrictors prevent their spread. When they reach the general circulation they are carried to the liver, where they are detoxified by esterases, as shown by perfusion experiments. Some detoxification also occurs in the blood by the same esterase.

Those local analgesics derived from para-aminobenzoic acid, e.g. procaine, benzocaine, butyn, larocaine, orthocaine and monocaine, are incompatible with the sulphonamides. The sulphonamides are taken up by the bacterial enzyme system using para-aminobenzoic acid, which in small amounts can antagonize the sulphonamides as wound antiseptics. Those drugs derived from para-aminobenzoic acid exert a similar action and should therefore not be used in the case of patients receiving sulphonamide therapy. Apart from inactivating the sulphonamides they interfere with their estimation and should not be used in obtaining samples of cerebrospinal fluid or other fluids for sulphonamide estimations. Nupercaine, amylocaine (stovaine), and metycaine are not derivatives of para-aminobenzoic acid and are therefore free from these objections.

Little is known of the mode of action of local anæsthetics. Sensory nerves are affected before motor and the size of the nerve fibre determines the degree of sensitivity to local anæsthesia. There is also some evidence that local anæsthetics act partly at the myoneural junction, like curare. It appears probable that a reaction catalysed by an enzyme system occurs between acetylcholine and creatine phosphate, and that this reaction occurs when an impulse travels along a nerve. This reaction is inhibited by local anæsthetics such as procaine, and this inhibition seems to be due to a competition between acetylcholine and procaine for the same enzyme receptors (Rapp, C. G., *Arch. Biochem.*, 1947, **12**, 13).

Another possible mode of action is based on the interference with the carbohydrate metabolism of nerve cells, which utilize carbohydrate exclusively for respiration. For carbohydrate breakdown enzyme systems containing members of the vitamin-B complex, and possibly para-aminobenzoic acid, are essential. It is possible that the local analgesics, is changed for one of 0·5% ethocain in 0·86% solution with 1/250,000 adrenaline and the entire field of operation surrounded by a subcutaneous injection. The line of incision is also infiltrated with the same solution, and to constrict the blood-vessels, a point just anterior to the sternomastoid at the level of the superior thyroid pole, and one towards the lower end of the thyroid gland, are selected for deep injection beneath the pre-tracheal muscles of 10 c.c. of the weak solution. This constricts the vessels along the anterior border of the sternomastoid and of the superior pole of the thyroid, and we have found in the large number of cases both of thyroidectomy and for gland dissection that the operative field is far less bloody and that it permits of a one-stage removal of such a lesion as carcinoma of the tongue, combined with a block dissection of the glands of the neck, without serious shock or interference with healing. We usually prefer pentothal for the stage of diathermy excision of the tongue, though it is possible for this to be done under block anæsthesia as well.

Dr. F. W. Roberts: In my experience very good anæsthesia for abdominal operations can be obtained by a bilateral mid-axillary intercostal block of D6-D12. I use a mixture of equal parts of 1% procaine and 1/1,500 nupercaine, placing 10 c.c. in each intercostal space.

With a gentle surgeon splanchnic block is hardly ever necessary. I do not believe that there is any justification for the use of posterior splanchnic block. Its technique is difficult: Lundy in his book "Clinical Anæsthesia" reports 52% failure. The possible complications are by no means trivial, and it must be done before the operation—before it is known whether it is in fact necessary.

In the cases in which, after intercostal block only, traction of the bowel is necessary and seems to upset the patient, an anterior splanchnic block can be performed by the surgeon with more accuracy and safety.

Dr. S. G. Ransom: I would like to express appreciation of Dr. Norman James' careful consideration of the patient's comfort. These various apparently small points make disproportionate difference to his well-being.

To the "unnecessary withholding of food" I would like to add "unnecessary assault by the enema". There is apparently no reason for it whatever from the point of view of the anæsthetic, not for a general, still less for a local one, and it does considerably add to the patient's distress, making him windy after the operation and often unhappy before.

Mr. Harold Dodd: I wish to describe a method of local anæsthesia for abdominal operations which has been used with consistent success since May 1937 in thousands of cases. It is a combination of local infiltration in the area of the incision and of the operation, plus regional infiltration in the abdominal wall and splanchnic sympathetic nerves. Its advantages are its simplicity and also its consistent effectiveness. It is my practice to demonstrate it to my House Surgeon on the first day and after two or three occasions he does one side of the abdomen while I do the other.

It is not a complete method of anæsthesia in itself. It needs to be supplemented by a general anæsthetic during the general exploration and during that part of the operation where handling viscera may occur, as for example during a partial gastrectomy. Once this is dealt with, the general anæsthetic may be discontinued, i.e. before the abdomen is closed. I prefer to supplement it with open ether or trickle doses of pentothal. Gas and oxygen are not quite so satisfactory because of the heaving respiration which it causes and patients' inclination to vomit as they come round, often on the table.

I would emphasize that the supplementation is a sleep and not a full anæsthetic. It is discontinued for instance before the abdomen is closed.

The distribution is as follows, the surgeon does the incision, and one side of the abdomen, whilst his assistant does the opposite side. Time must be given for the anæsthetic to act; the anæsthetic medium is 1 : 1,000 amethocainewhich is sterilized by the autoclave and then 1 minim of 1 in 1,000 adrenaline is added to each ounce of anæsthetic immediately before use. The volume which may safely be used is 200 c.c. followed ten minutes later by a further 100 c.c. I have never seen any ill-effects from the use of this drug. It requires five minutes to produce anæsthesia. Before making the anterior splanchnic injection great care is taken to aspirate with the syringe. This ensures that the needle point is not in one of the large vessels in this area. Should blood be withdrawn the needle is taken away, pressure is applied with a firm swab for three minutes and the injection is remade.

Finally, a note on the size of the needle used. I find that a No. 15 hypodermic needle is best, and being short it makes the possibility of perforation of the peritoneum and puncture of the bowel slight. I always use a 5 or 10 c.c. syringe. This allows delicate work and does not fatigue the hand before the operation.

The following figures were shown and are to be seen in the *Post-Graduate Medical Journal*, 1946, 22, 389, "Local Anæsthesia for Abdominal Operations," by H. Dodd, Ch.M. (A Reprint will be supplied on request to Mr. Dodd, 42, Harley St., W.1.)

Having made the brachial plexus block, the patient is gently rolled over on to the sound side, or, as I personally prefer, on to the face, and an intercostal block, using 0·75% of ethocain in normal saline, which in this instance should be 0·75% in strength, given, containing 1/250,000 adrenaline. The block is carried out three fingerbreadths or about 4 cm. from the spinous processes, and must be carefully carried out in order to be sure of missing no intercostal nerve. 2, 3, 4, 5, 6 and 7 are injected, sometimes 8 as well, but it is an advantage to locate the first rib without injecting 4 cm. from the mid-line and opposite the seventh cervical spinous process (vertebra prominens). 10 c.c. per nerve is ample, and in order to avoid missing a nerve, two 8 cm. needles are used, one remaining in situ whilst the second needle leapfrogs from rib to rib until all six nerves have been injected. When this is completed the patient is again rolled gently on to her back and a solution of 0·5% ethocain in 0·86% saline with 1/250,000 adrenaline is used to surround the field of operation. A little over 1 c.c. of solution is used per cm. of the line extending along the whole length of the clavicle, down the middle line of the sternum along the costal margin, and along the eighth rib as far as the latissimus dorsi. In stout patients rather more solution is injected than in thin, the subcutaneous injection along the sternum should be especially generous since it is desirable to block the anterior perforating branches of the intercostal nerves on the healthy side to allow sufficient under-cutting. This concludes the measures necessary to secure analgesia.

The remaining solution must contain 1/250,000 adrenaline but need contain only 0·25% of ethocain. It consists of: First, injection into the anterior ends of the second, third and fourth intercostal spaces. This should be made with the needle point in contact with the deep surface of the costal cartilages and is designed to constrict the internal mammary artery with its principal perforating branches.

Second, an injection of 10 c.c. is made into the pectoralis major muscle at the level at which the surgeon will subsequently divide it.

Third, an injection is made deep to the pectoralis major and at the level of the upper border and of the lower border of the pectoralis minor muscle (10 c.c.). This is designed to constrict the pectoral and humeral branches of the acromio-thoracic artery, and also the long thoracic artery which runs along the lower border of the pectoralis minor muscle.

Fourth, injections are made on the chest wall of the axilla as high up as can be reached into the intercostal spaces in contact with the ribs. This is designed to constrict the lateral perforating branches of the intercostal vessels.

Lastly, an injection is made of 10 c.c. of the weak solution along the latissimus dorsi muscle, designed to constrict the trunk and branches of the long subscapular artery.

The patient will be ready for the operation to start as soon as these injections have been completed. No other injections are necessary, and in nearly all cases the patient slumbers peacefully during the operation. Blood loss is very greatly reduced, and we have found that shock, which is sometimes an alarming feature of a breast operation, has not been apparent.

The neck: In this region operations for removal of thyroid gland and for block dissection of glands of the neck are greatly facilitated by a relatively bloodless field, and by the absence from the vicinity of the operative field of an anæsthetist and his impedimenta.

I have used the lateral oblique route of Meeker and Hundling for cervical plexus block so often as to feel quite sure that the risks and occasionally reported fatalities from cervical plexus block are due to either intravenous or high intraspinal injection, and I have not only used this technique myself, but have had it done for me by three different anæsthetists and by house surgeons, and it has appeared to me as safe and eminently useful.

If the injections are made at a 45 degrees angle from above downwards, it is impossible to penetrate the spinal canal, and the usual precautions of using an unmounted needle and of aspirating before injecting will eliminate the risk of intravenous injection. The patient must be adequately premedicated, and in the case of toxic goitres a small dose of adrenaline should be given on the previous day to test for idiosyncrasy to this drug. In my experience real idiosyncrasy to adrenaline is uncommon.

The patient lies on her back with the face turned away from the side which is being injected. The tip of the mastoid process and the line of the cervical transverse processes are defined by palpation. Wheals are raised at the level of the tip of the mastoid 1·5 cm. below and 1·5 cm. below this again. The needle is inserted towards the line of the transverse processes and obliquely downwards towards the foot at an angle of 45 degrees. As soon as contact is made with bone, aspiration is carried out, and then 5 c.c. of 0·75% ethocain in 0·75% saline with 1/250,000 adrenaline are injected whilst the needle is moved to and fro through a distance of about one-half cm. When this is done, the remainder of the contents of the 10 c.c. syringe is injected as the needle is withdrawn towards the subcutaneous tissue. This first injection should reach the transverse process of the second cervical vertebra at the point where the downward sloping gutter between the anterior and the posterior tubercles gives attachment to the anterior and posterior inter-transverse muscles.

Having injected the second, third and fourth cervical nerves on the two sides, the solution

Section of Pædiatrics

President—DENIS BROWNE, F.R.C.S.

[*February* 28, 1947]

Lipodystrophy.—M. E. MACGREGOR, M.D. (for URSULA JAMES, M.R.C.P.).

A. W., 17.6.46: Brought to Victoria Hospital for Children, then aged 8 months, because of wasting of the limbs dating from birth.

Past history.—First child. Full term. Normal delivery. No asphyxia. Birth-weight 5½ lb. Breast-fed for six months. Circumcised at one week. No illnesses. Said to have lost 1½ lb. in first three days of life, but to have been ½ lb. above birth-weight by end of third week. Thereafter gained steadily. 14 lb. at time of first attendance. No *family history* of disease. From birth his limbs, especially legs, had been thin. Strength apparently normal and movements free.

On examination.—Limbs muscular. Little subcutaneous fat on legs, its lack being most pronounced distally. Some deficiency of fat in forearms also. Symmetrical distribution of fat loss. Hands and feet rather long. Face and trunk normal. Power of limbs and tendon reflexes normal. Mental and physical development otherwise normal for age.

Investigations.—X-ray of limb bones and electrical reactions of muscles of arms and legs were normal.

Diagnosis.—Lipodystrophy of unusual distribution. No treatment prescribed.

17.2.47: Weight 18½ lb.; age 16 months. Very healthy. Walks and has started to talk. Takes full mixed diet. Condition of limbs unchanged, but fat deficiency in legs and forearms is now more conspicuous.

Dr. Parkes Weber said that this case was unlike any previously shown to the Section or to the Society for the Study of Diseases in Children. It was obviously a congenital defect in the development of fat and thus probably different from the ordinary cases of lipodystrophy.

Congenital Defect of the Scalp.—SIMON YUDKIN, M.B., M.R.C.P. (for H. M. M. MACKAY, M.D., F.R.C.P.).

C. S., aged 4½ years.

History.—Birth-weight 4 lb. 4 oz., V.L.O.A. after a long but otherwise normal labour. At birth there were four areas on the vertex where the skin was absent. The areas were covered with granulation tissue and the edges appeared to be healing. The largest area was over the sagittal suture; there was a small area just in front of this, a third area over the posterior fontanelle and a small fourth area just behind this. The skull was deficient under the largest area as though the sagittal suture were very wide, and the posterior fontanelle was noted to be about twice the normal size.

Heart.—There was a soft systolic murmur at the apex.

Fig. 1.—Local anæsthesia of the upper abdomen as for a gall-bladder and stomach or an upper abdominal procedure.—It illustrates the local infiltration for a right paramedian incision. On the left side the numbers refer to the intercostal nerves. On the right side they refer to the volume of local anæsthetic injected; this may be increased to 10 c.c. at each point. The point of the seventh nerve is half-way between the ensiform cartilage and the intersection of the costal margin with the linea semi-lunaris.

Fig. 2 shows the method of subcuticular and deep injection for the local infiltration.—The needle is injecting subcuticularly 3 c.c. and is then almost withdrawn and reinserted vertically introducing a further 3 c.c. into the full thickness of the abdominal wall with pooling in posterior rectus sheath. The needle is kept as closely subcuticularly as possible to raise a wheal not as in this diagram.

Fig. 3 demonstrates the arrow-head injection.—The right side shows the correct method. The syringe is kept horizontally so that the needle may penetrate the full thickness of the flank. The left side shows how only part of the abdominal wall is infiltrated if the needle is introduced obliquely.

Fig. 4 outlines the local and regional injection for suprapubic cystostomy.—The former consists of the lower three-quarters of the mid-line between the umbilicus and the symphysis pubis. The latter is the arrow-head injection on both sides.

Fig. 5 indicates the local and regional injection for inguinal and femoral herniæ.—The local infiltration is superficially and deeply in the line joining the anterior superior iliac spine to the pubic spine. The regional insertion is the arrow-head injection on the side of the hernia, 10 c.c. in each direction.

NOTE.—The incision is from anterior superior iliac spine to pubic spine.

Fig. 6 gives the local and regional infiltration for appendix operations or colostomy (left side).—Incision for appendix operations (right side) or colostomy (left side) was indicated. The heavy line shows place of the incision which is infiltrated from the arrow-head injection to the pubic spine. All the structures of the abdominal wall may be divided in this line.

Fig. 7 illustrates anterior splanchnic anæsthesia.—The needle is introduced at the upper border of pancreas in the mid-line between the aorta on the left and the inferior vena cava on the right. The shadow of each is visible through the posterior parietal peritoneum. 40 c.c. of anæsthetic are pooled here. To expose the pancreas, the stomach is held down by the operator's left hand and swab as per the diagram. The liver is elevated by a Pannett's retractor.

Fig. 8 tells of local infiltration of the stomach.—On the right of the stomach note the insertion of 10 c.c. above and below the pylorus thus blocking the pyloric and right gastro-epiploic arteries. To the left a further 10 c.c. are injected at the lower pole of the spleen to insulate the nerves with the left gastro-epiploic artery. Just below the cardio-œsophageal junction exactly on the edge of the lesser curvature 10 c.c. of anæsthetic is pooled to neutralize the right and left vagus; the anæsthetic tracks round to the anterior and posterior surfaces of the stomach.

Fig. 9 points out the local infiltration for biliary tract operations.—The needle was introducing 10 to 15 c.c. into the gall-bladder bed. This allows stronger traction to be exerted on the gall-bladder thus revealing the common bile duct around which a further 10 c.c. of anæsthetic is introduced subperitoneally as indicated by the arrow.

Dr. Stanley Rowbotham (President): The problem of sedation with local anæsthesia has always baffled me. I have tried many of the barbiturates, but they have not, in my hands, proved wholly successful. I have used a product called "Pernocton" (not obtainable since the war) which kept the patient lightly asleep for a considerable time without excitement such as occurred during the elimination of many of the other barbiturates. On the whole I found that chloral hydrate by the mouth combined with small doses of omnopon subcutaneously gave the best results.

I have never undertaken to anæsthetize for radical breast operation by local alone, because I felt it would prove such an ordeal for the patient. Speaking of the cervical plexus block for thyroidectomy, I have personally anæsthetized a great many cases by this method, but I have not found it so successful as a properly performed infiltration. Mr. Molesworth, in fact, has said that he used local infiltration in addition to his cervical plexus block.

Referring to Mr. Harold Dodd's remarks, he (the President) could see no reason for using a solution of amethocaine stronger than 1 : 4,000. He found the posterior approach to the splanchnic area without difficulties, and equally effective as that performed after the abdomen had been opened.

13.1.47: X-ray. Further absorption of pneumothorax, with clearing of underlying lung. Physical signs: General condition very satisfactory; respirations quiet. Chest: No physical signs.

The interest of this case lies in the differential diagnosis and radiological progress of the cyst, there being three main possibilities, namely:

(1) A congenital cyst, (2) an encysted pneumothorax and (3) a pneumatocœle, in each case rupturing to form a generalized pneumothorax.

Congenital cyst is said to be a very rare anomaly, indeed its very existence is denied by some authorities who hold it to be invariably an acquired emphysematous condition, thus merging with the third diagnosis.

Encysted pneumothorax does not conform to the radiological findings which show the lung tissue curving round the periphery of the cystic area and the compression of the hilar structures typical of a cyst.

The most likely diagnosis is therefore that of a pneumatocœle. The pneumatocœle occurs during the course of a pneumonia, as in this case, the mechanics producing it being a check-valve bronchial obstruction caused by swollen mucosa leading to the formation of an obstructive emphysematous cavity. In this case there was certainly one such cyst, possibly two; the large definite one appearing in the area showing the signs of pneumonia. The cyst ruptured to form a pneumothorax, a phenomenon which as far as can be ascertained occurred in only two other cases of pneumatocœle, these being reported by Benjamin and Childe. The herniation of the pneumothorax across the mediastinum accompanied by the slight shift of the mediastinum confirmed the supposition that the air in the cyst was under tension. This is in keeping with the findings of Lister of America who demonstrated a positive pressure in these cysts by manometric measurements in the living subject. The uneventful recovery of the infant after the initial pneumonic attack was overcome is also in keeping with the case histories of other pneumatocœles.

In the discussion which followed, other similar cases of pneumatocœles occurring in older children were mentioned; these, however, had disappeared without any complications such as pneumothorax. Dr. Wyllie was surprised that the cyst had remained uninfected, attributing this to the early treatment with chemotherapy. Actually all the literature on the subject emphasizes the rarity with which these cysts are involved in complications, pointing out that they nearly always disappear spontaneously with no ill-effects either at the time or afterwards.

Traumatic Periostitis.—R. M. TODD, M.D., M.R.C.P., D.C.H.

P. J., female, aged 2 years 3 months.

History.—10.12.46 to 18.12.46: In hospital for septic area of skin overlying the right tibia. Treated with sulphathiazole by mouth and mag. sulph. locally.

22.12.46: Taken to hospital because of inability to walk on right leg. X-ray showed spiral fracture. Right tibia put in plaster. One week later plaster was removed because of painful swelling of right thigh.

6.1.47: Transferred to Queen Elizabeth Hospital for Children as case of osteomyelitis.

Past history.—No history of injury. Teething normal—no bleeding from gums. Never had cod-liver oil or orange juice at home, but has attended nursery. Has had fresh fruit when available.

On examination.—6.1.47: T. 99·6°, P. 120, R. 20. Flushed: Bruise on right side of face. Legs—Left: Slight pain on movement, no redness or swelling. Right: Lying in position of rest. Skin overlying lower end of femur, red, shiny and hot. Obvious swelling. Area of thickening over upper third right tibia. Nothing abnormal elsewhere.

Provisional diagnosis.—Osteomyelitis of right femur.

Course of penicillin commenced—30,000 units I.M. four-hourly for two weeks.

The ulcers healed well in about three weeks, and at the age of 4 months the anterior fontanelle was noted as being normal although the posterior fontanelle was still larger than normal.

Development was fairly normal although he has always been small for his age. X-ray examination at 1 year 8 months—skull, heart, long bones normal.

Family history.—Only child. Parents alive and well. No similar condition in any of the family.

On examination.—A healthy-looking boy, rather small for his age (weight 30 lb.). Scalp: Four areas of scar tissue with much keloid. Each area symmetrical in relation to skull mid-line.

There is still a systolic murmur at the apex.

Comment.—The symmetry of these lesions and their usual multiplicity, the fairly frequent presence of other congenital abnormalities, the occasional familial occurrence and the absence of any evidence of intra-uterine injury or amniotic adhesions suggest that they are developmental in origin. Ingalls has described several human embryos with a bullous area in the midline of the skull which appears to be the early stage of these defects.

The President said that a rather similar type of lesion could be caused by pressure due to prolonged labour and early loss of the amniotic fluid; these two types of lesions may be confused.

Dr. Parkes Weber thought that in this case the type of healing indicated an intra-uterine injury rather than a developmental defect.

Dr. Helen Mackay pointed out that these congenital defects of the skin were probably not rare, although usually small and so receiving little attention. A familial tendency was sometimes observed.

Pneumatocœle Occurring During Pneumonia and Rupturing to Form a Pneumothorax.—

JOSEPHINE HEBER, M.B. (for H. M. M. MACKAY, M.D., F.R.C.P.).

S. C., born 6.7.46. Normal pregnancy and delivery; birth-weight 7 lb. 12 oz.

Well until 7.12.46 when she was admitted to hospital, extremely ill, with very rapid and distressed respirations and marked cyanosis. T. 101°. Alæ nasi working. Chest: Signs of consolidation at right base.

Investigations.—10.12.46: R.B.C. 4,700,000, Hb 88%, W.B.C. 24,000, (P. 74%, L. 18%, M. 8%). 11.12.46: Throat swab. Moderate growth of *B. friedländer*.

Treatment.—Oxygen tent. Sedatives: Chloral 1 to 2 grains p.r.n. Chemotherapy: (*a*) Penicillin 10,000 units four-hourly, increased to 20,000 units four-hourly. (*b*) Sulphadiazine 0·5 gramme four-hourly, started at once.

Progress.—Remained extremely ill, with respirations of 90 to 100, for four days, after which slow improvement occurred. No abrupt changes. Temperature remained high, then slowly settled over fourteen days. Child too ill to X-ray initially. Physical signs slowly disappeared.

21.12.46: W.B.C. 12,000 (P. 22%, L. 56%, M. 14%). Sulphadiazine discontinued.

23.12.46: X-ray. Large unilocular air-containing cyst at right base. Remainder of lung appears compressed suggesting positive tension within the cyst. Mediastinum central. Physical signs: Dullness and diminished air-entry at right base.

28.12.46: X-ray. The air cyst at right base now ill-defined. Large mainly apical right pneumothorax present, with herniation of the upper anterior mediastinum across the mid-line and slight displacement of mediastinum to left. Partially collapsed lung shows irregular trabecular shadows. Left apical cyst has disappeared. Physical signs: No hyper-resonance. Dullness and diminished air-entry at right base.

30.12.46: X-ray. Right pneumothorax considerably less, with marked expansion of the underlying lung. Mediastinum central. No evidence of air-cyst.

9.1.47: X-ray. Small apical pneumothorax remains. Mediastinum now drawn to right. Penicillin discontinued.

(5) *Traumatic.*—Ossifying periostitis due to trauma in infants within the first three months of life is a well-known syndrome (Snedecor, Knapp, and Wilson, 1935) and is due to birth trauma and occurs particularly in breech deliveries. It can also occur in older children (Tietze's disease).

Conclusions.—Although there was no history of trauma in this case, the presence of spiral fractures of the tibiæ and a damaged right femoral epiphysis, and the subsequent clinical improvement with radiological signs of healing, confirm the diagnosis of traumatic periostitis.

REFERENCES

CAFFEY (1946) *J. Pediat.*, 29, 541.
CASS (1940) *Arch. Dis. Childh.*, 15, 55.
SMYTH, POTTER, and SILVERMAN (1946) *Amer. J. Dis. Child.*, 71, 333.
SNEDECOR, KNAPP, and WILSON (1935) *Surg. Gynec. Obstet.*, 61, 385.

Hyperelasticity of Skin.—E. M. KINGSLEY PILLERS, M.B. (for RICHARD DOBBS, M.R.C.P.).

V. R., aged 3½ years.

History.—Admitted for investigation of puffiness of hands and feet, and observation of mental capacity. *Family history.*—Nothing relevant known. Parents uninterested in the child who has recently been living with friends.

On examination.—Nervous and apprehensive. Intelligence probably normal. On admission there was marked puffiness of the hands which gave the appearance of a rubber glove filled with water. There was similar swelling on the dorsum of the feet. The finger-joints show hypermobility and this is present to a lesser extent in the toes which have deformed nails. The palate is high. At the sides of the apparently short neck are large folds of skin, which, when stretched, give a webbed appearance to the neck. Movements of head and neck normal. General physical examination revealed nothing abnormal.

Investigations.—Hb 84%, R.B.C. 5,000,000, W.B.C. 10,500. Blood cholesterol 175 mg.%.

X-ray long bones N.A.D. X-ray cervical spine: No Klippel-Feil deformity. Failure of formation of ossific centre for the upper anterior vertebral body margin of C5. Biopsy of skin: Normal histological structure.

The interest in this case lies, I think, in the diagnosis of which three possibilities must be considered: Klippel-Feil syndrome, Ehlers-Danlos syndrome and pterygium colli. Although bearing a superficial resemblance to a Klippel-Feil syndrome, the normal mobility of the neck and the X-ray of the cervical spine clearly eliminate this as a possible diagnosis. In Ehlers-Danlos syndrome three characteristics are usually found: hyperelasticity of the skin, hypermobility of the joints of the fingers and evidence of increased capillary fragility as shown by numerous bruises and cuts. This child shows the first two features of the syndrome but there is no evidence whatever of increased capillary fragility and the patient has had plenty of falls and minor injuries while playing with other children. In the previous cases of pterygium colli reported by De Briun and Kobylinski stress is laid that the folds at the sides of the neck are due to lack of skin in the cervical region. Normally the skin stretches perpendicularly downwards from the mastoid to the clavicle and then laterally from this point to the acromion. In these cases of congenital webbing, the skin is short and when the neck is rotated it is forced to bridge the distance from the mastoid to the acromion in a straight line. When, however, the neck is not rotated the folds are loose and feel soft. Other congenital abnormalities known to be associated with pterygium colli are also found in this case. I think the puffiness of the hands and feet may be due to congenital lymphangiectatic œdema, the palate is high, the toe-nails are deformed and as already noted there is hypermobility of the joints of the fingers and toes.

Investigation and progress.—7.1.47: T. 101·6°, W.B.C. 10,000 (metamyelocytes 3%, stabs 18%, polys. 36%, lymphos. 36%).

11.1.47: Temperature normal. Hb 80% (11·02 g.), R.B.C. 4,200,000, C.I. 0·9, W.B.C. 4,000 (stabs 9%, polys. 21%, lymphos. 61%), E.S.R. 3 mm. in one hour, platelets 156,000 per c.mm. Urine—No red cells: Ascorbic acid excretion 10 mg. in fourteen hours. Marked clinical improvement. Left leg normal. Right leg less swollen and tender. Temperature normal.

15.1.47: Bleeding time 50 seconds: Coagulation time one and a half minutes. Right thigh only slightly painful, not red, swelling still present.

21.1.47: Bony thickening of right femur, not tender. W.B.C. 10,000 (stabs 12%, polys. 45%, lymphos. 37%).

2.2.47: Walking round cot. No tenderness of legs. No pain on movement. W.B.C. 7,000 (polys. 42%, lymphos. 52%), E.S.R. 3 mm. in one hour.

12.2.47: W.B.C. 9,200 (stabs 3%, polys. 35%, lymphos. 54%).

X-ray appearances.—7.1.47: *R. femur*, diffuse subperiosteal new bone deposition over the lower two-thirds of the femoral shaft. There appear to be at least three separate layers of new bone and inferiorly the epiphyseal line is crossed. There is no evidence of fracture but slight posterior displacement of the lower epiphysis is not excluded.

R. tibia, there is an obvious spiral fracture involving the middle two quarters of the shaft of the bone. Position satisfactory. Moderately well-established callus is present.

L. tibia, 11.1.47: There is what appears to be a fracture line in the upper part of the L. tibia. 21.1.47: There is now a definite fracture of the upper part of the L. tibia and obvious periosteal reaction in the mid-shaft region.

X-ray conclusions.—The appearances are most easily explained by a traumatic ætiology producing spiral fractures of both tibiæ and damage to right femoral epiphysis with subperiosteal hæmorrhage spreading up the shaft of the femur.

Comment.—This case presented an interesting problem in diagnosis and the following possibilities have to be considered:—

(1) *Metabolic.*—The radiological appearance of subperiosteal hæmorrhage becoming calcified suggested the diagnosis of scurvy. Against it were (*a*) the absence of scorbutic changes in the gums and ribs, and the absence of red cells in the urine; (*b*) the presence of 10 mg. ascorbic acid in a fourteen-hour specimen of urine; (*c*) the absence of epiphyseal scorbutic changes.

(2) *Infective.*—(*a*) Syphilis—there were no clinical signs of spirochætal disease and Wassermann and Kahn reactions were negative; (*b*) osteomyelitis—multiple lesions are common in osteomyelitis of the newborn (Cass, 1940) and in these cases constitutional disturbance is minimal and prognosis is good. The age of this child was against the diagnosis, and white count and sedimentation were normal; (*c*) infection elsewhere in the body, e.g. intrathoracic lesions can give rise to extensive periosteal new bone formation which often has a laminated appearance as in this case. Against the diagnosis was the absence of clinical and radiological evidence of infection.

(3) *Neoplastic.*—In periosteal sarcoma the shaft of the bone is unaffected and there is rapid local and metastatic spread. Ewing's tumour can produce a similar radiological "onion-like" appearance. In this case the general condition of the child and the radiological picture were against a neoplasm.

(4) Recently a new syndrome occurring in children up to the age of two and a half years has been described by Smyth, Potter, and Silverman (1946) under the title "Periosteal Reaction, Irritability, and Fever in Young Infants", and by Caffey (1946) as "Infantile Cortical Hyperostoses", in which there is periosteal reaction in multiple bones. The facial bones are usually involved producing a characteristic facies. All the cases recover, but in the 17 recorded cases there was no evidence of fractures.

Biochemical examinations (Dr. W. W. Payne): Van den Bergh's reaction normal. Thymol turbidity ++ (19 units). Takata-Ara ++. Blood urea 18 mg. per 100 c.c. Blood cholesterol 245 mg. per 100 c.c. (The two brothers 160 and 181 mg. per 100 c.c.) Glucose tolerance and adrenaline curves normal. B.M.R. +4%. E.E.G. shows diffuse, fast and slow dysrhythmia and suggests idiopathic epilepsy.

The differential diagnosis was discussed and an idiopathic xanthomatosis suggested as most probable.

POSTSCRIPT.—Splenectomy and liver biopsy were performed by Mr. Charles Donald. Pathological report (Dr. M. Bodian):—The liver showed definite evidence of periportal cirrhosis. The liver cells were normal in appearance. The spleen showed moderate thickening of capsule and trabeculæ, and a rigid network of thickened reticulum in the pulp. The thickening of the reticulum was due to proliferation of reticulum cells and thickening of reticulin and collagen. These findings are indicative of Banti's syndrome.

Dr. Parkes Weber said that this might be familial Gaucher's disease and the abnormality of the phalanges might be due to minute collections of Gaucher cells. Another possibility was that the case might be one of the, as yet, imperfectly recognized lipoidoses.

DEMONSTRATION: DIAGNOSIS OF THREADWORMS

By J. M. WATSON, D.Sc., A.R.C.S., and R. C. MAC KEITH, D.M., M.R.C.P.

(*Wellcome Laboratories of Tropical Medicine & Institute of Child Health, University of London*)

INTRODUCTORY NOTE.—The accurate diagnosis of threadworm infestation depends on the recovery of the ova from the perianal skin. The clinical picture is unreliable for diagnosis and eggs are but rarely found in the fæces as the mature female worms emerge from the anus to oviposit on the neighbouring skin. Many devices have been used to recover the threadworm eggs from the perianal skin. Hall (1937) evaluated the comparative efficiency of those in use at that date and showed that swabs of cotton, chamois and rayon, and scrapers of celluloid, wood and metal were unreliable. He introduced the NIH cellophane swab which proved more convenient and more reliable than anything previously employed. Since that date several other methods of diagnosis have been introduced, some of which had certain advantages over the NIH swab. In a forthcoming paper it is proposed to record the results of controlled laboratory experiments and clinical trials designed to evaluate these diagnostic techniques. The demonstration was designed as a preliminary report making available some of our experience as to the relative practical usefulness of the methods. Only those which have proved to have definite individual advantages are described here.

(1) *NIH swab* (Hall, 1937).—A piece of transparent cellophane 3 × 1½ cm. is folded on the rounded end of a 4 mm. glass rod and held in position by a rubber band. The other end of the rod is inserted into a rubber stopper and the whole inserted into a 7/8 in. glass test tube for the protection of the swab in transport. The swab is applied to the perianal skin of the patient. The cellophane is removed and flattened on a drop of decinormal sodium hydroxide solution on a slide, two drops being placed on it and the preparation covered with a coverglass.

(2) *TP swab* (Watson and Mac Keith, 1946).—This device employs toilet paper in place of cellophane; the paper being applied with the finger or using a glass rod as with the NIH swab. The paper is rendered transparent by placing it, applied surface upwards, on a drop of clearing agent such as oil of wintergreen, another drop being added and the preparation covered with a coverglass. The eggs clear much more slowly than the paper and are readily visible against a translucent background.

(3) *Glass pestle* (Schuffner and Swellengrebel, 1943 and 1944).—For the pestle originally described we find a thick-walled test tube may conveniently be used, the lower end being roughened on a grinding wheel. For use the pestle tip is moistened with water and applied firmly with rotary motion to the perianal skin for about ten seconds. The ova, including those in the perianal folds, which may be missed by NIH or TP swabs, form with epithelial cells an emulsion which is transferred to a slide. It may either be covered with a coverslip and examined at once or else allowed to dry and examined at leisure after clearing with cedarwood oil or Monnig's medium.

(4) *Adhesive cellophane or Graham swab* (Graham, 1941).—3/4 or 1 in. cellophane adhesive tape is used. A 1½ in. length is applied to the perianal skin on the finger or on a glass rod as with the NIH swab. After application the tape is flattened on a glass slide to which it sticks. Examination may be direct but is facilitated by running a little decinormal sodium hydroxide solution under the

Dr. Parkes Weber said that Ehlers-Danlos syndrome consisted of cutis laxa, hyperextensibility of the joints and excessive friability of the cutis. The child in this case showed the first two features and was therefore an example of an incomplete form of this syndrome.

Cystic Disease of Bone.—N. F. ELLIOTT BURROWS, B. M. (for BERNARD SCHLESINGER, F.R.C.P.).

J. F., aged 6 years. Fourth child of normal parents. No relevant family history.

Quite well till October 1945 when he fell and fractured his right arm. Two days later fell again and refractured same area. X-ray revealed cysts of several bones, right humerus, radius, femur and tibia. Blood chemistry at this time: Calcium 10·4 mg., phosphorus 3·6 mg., alkaline phosphatase 27·5 units per 100 c.c. Fractures healed well.

Eight months later readmitted with fracture of right radius following a fall. Blood chemistry repeated showed practically identical figures to the previous estimations.

Dr. Herbert Levy suggested that the possibility of Rhesus incompatibility should be considered in these cases of polyostotic fibrous dysplasia (cf. H. Levy, *Brit. med. J.*, 1942 (ii), 738).

Dr. Parkes Weber said that this was obviously an example of osteitis fibrosa multiplex, i.e. it was of the same nature as the single fibrocystic lesions and was not due to parathyroid abnormality. Multiple instead of single cysts were present in the "multiplex" cases which might be termed "polyostotic focal fibrocystic dysplasia".

Hepatosplenomegaly.—J. P. M. TIZARD, B.M., M.R.C.P. (for DONALD PATERSON, F.R.C.P.).

V. T., female, aged 7 years.

History.—First-born child. Milestones delayed; always backward. No relevant illness until one year ago, when she had a single convulsion during a cold. Three further fits in January 1947 when she was otherwise in good health.

Family.—Two brothers aged 5 and 2 years, who are perfectly well and of normal intelligence. Both have livers palpable respectively two and three finger-breadths below the costal margin. Mother and father alive and well.

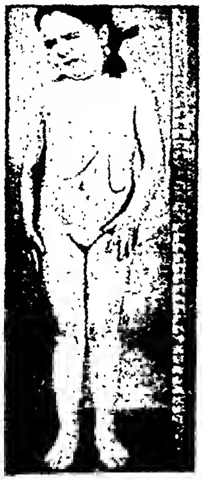


FIG. 1.

On examination (*see* fig. 1).—Height 46½ in. Wt. 58½ lb. Head circumference 20½ in. Dull expression, overhanging forehead; slow mentally and physically; spatulate hands, toes irregular in size, no lordosis, no limitation of joint movement. Coarse pale skin; slight icterus when first seen. Teeth widely spaced and carious. Protuberant abdomen; liver enlarged three finger-breadths, firm and smooth; spleen enlarged half-way to umbilicus; no ascites. Hypermetropia; no corneal opacities; fundi normal; deep reflexes sluggish.

Radiographs (Dr. F. L. Ingram).—Skull normal; long bones and spine normal; metacarpal bones and phalanges show irregularity of length and texture suggestive of enchondromatosis. (No abnormalities found in corresponding radiographs of the brothers.)

Investigations.—Blood examination (Dr. I. A. B. Cathie): 10.2.47: R.B.C. 3,670,000 per c.mm., Hb 80%, W.B.C. 6,300 (normal differential), reticulocytes 1·2%, red cell fragility normal, platelets 105,600 per c.mm.

28.2.47: R.B.C. 4,400,000 per c.mm.

Sternal marrow, leuco-erythroblastic ratio 3·5 : 1, otherwise normal.

Rhesus factor: Patient, Group A, Rh-positive; both brothers, Group A, Rh-negative; mother, Group A, Rh-negative, no antibody detected; indirect Coombs' test negative; a biological test cannot be carried out now as she is pregnant.

C.S.F. normal. Blood W.R. and Kahn negative.

With regard to the use of barbiturates as basal anæsthetics, allowing the patient to be brought to the theatre in an unconscious state, yet not sufficiently depressed for surgical procedures, I would like to stress the need to give sufficient of the barbiturate chosen. To do otherwise will bring disappointment, the child will often be in a wild, unmanageable state and induction of anæsthesia can be more difficult than if no drug had been given at all. It is probable that a dose of nembutal 0·7 grain per stone or seconal 0·75 grain per stone will be satisfactory. An injection of atropine should follow half an hour later.

The Induction and Maintenance of Anæsthesia in a Few Specific Surgical Procedures:

(1) *Tonsillectomy and adenoidectomy.*—This is still the commonest operation performed at any children's hospital. For this reason it is interesting to note that at Great Ormond Street neither the technique of the operation nor of the anæsthetic has changed very much since 1907. In that year Waugh, with the help of Sington, a past President of the Anæsthetic Section, began to dissect the tonsils and curette the adenoids under deep chloroform. Later a change was made to deep ether, using air or oxygen as its vehicle, for the anæsthetic agent. The vapour is delivered to the patient's mouth by a hooked metal tube, whose design has not changed since Waugh first described the operation. The airway is maintained by Waugh's gag whose jaws are made of small blocks of lead which fit snugly on the molar teeth, and the tongue is drawn firmly out of the mouth by a large pair of tongue forceps held by a nurse.

(2) *Abdominal surgery.*—In young babies the most frequent reason for a laparotomy is the condition of congenital pyloric stenosis. Some surgeons have excellent results with Ramstedt's operation, using local anæsthesia, others can point to a high degree of successful results using general anæsthesia. Ether and oxygen is the routine general anæsthetic used, and one is struck by the absence of post-operative complications when using ether. In addition, it is a personal opinion that the same good results are obtained by using ether on the other acute abdominal catastrophes of babies, for example, exomphalos, duodenal atresia and later intussusception. For these ill babies it has been my experience that the patient is brought more smoothly to a deep plane of anæsthesia if induction is performed with ether alone or with di-vinyl ether. Maintaining a perfect airway in these babies used to cause me anxiety, and I would therefore like to mention the very great help I have had from passing a No. 0 or 00 Magill tube through the mouth. All the advantages of the Magill tube in adult abdominal surgery are at once brought into play, and I do not think the delicate baby's larynx has suffered.

Etherington Wilson and others have described the use of spinal anæsthesia for babies undergoing major abdominal surgery. Bearing in mind the absence of post-operative complications in babies after general anæsthesia it has seemed safer to me to employ the latter method. This choice may be because I have not had sufficient experience in spinal injections on children. It will therefore be helpful to hear the views of others who have had more experience in this technique.

Hirschsprung's disease.—The neurological theory of autonomic imbalance as the causation of this condition is well known as is also the work of Telford (1939) who first used spinal analgesia in this condition here. This work has been continued since 1939 and described by Hawksley (1944). Cases treated by high spinal analgesia have also been described before this Society by Hawksley (1943), and by Court and Hasler (1942). Due to the war my own experience is small; it began in 1945 and is limited to 10 cases. I personally find paralysis of the whole sympathetic supply of the colon, which has been shown to reach as high as the 5th thoracic segment, to be more certain by using the Howard Jones method of dosage for nupercaine 1 in 1,500 solution. The youngest patient in my own series was 20 months.

The subject of autonomic nervous system imbalance does not end with Hirsch-tape and between it and a superimposed coverglass. The NaOH is unnecessary where the cellophane is applied with the finger, as in this case it is not dry and easily lies flat on the slide.

(5) *Direct slide* (Petersen and Fahey, 1945).—An ordinary 3 × 1 in. glass slide is pressed against the anal mucocutaneous junction so that one edge of the slide is towards the centre of the anus. The opposite edge of the slide is similarly applied to the opposite anal margin. The eggs adhere to the slide. The slide may be examined direct or after addition of a clearing agent or decinormal sodium hydroxide solution.

(6) *Brush* (Watson and Mac Keith, 1946).—This is an adaptation of the method of Nolan and Reardon (1939) for collecting household dust for examination for threadworm eggs. The small camel-hair brush is moistened with water and applied to the folds of the perianal skin with a stroking motion. For examination it is gently dipped into a few drops of decinormal sodium hydroxide solution in a deep well-slide. Any eggs present collect at the bottom of the well-slide, and are quickly found.

(7) *Vaselined cloth* (Hellsten, 1933).—This method is mentioned as it was omitted in Hall's (1937) review.

In replying to the discussion **Dr. Ronald Mac Keith** said that in deciding which is the best of these methods one had to consider the qualities of the devices: Reliability, simplicity of use (especially if parents are asked to do the necessary serial tests on the child or on themselves), ease of preparation and of cleaning for further use, and simplicity of examining the slide or preparation for ova. The NIH swab is sometimes inconvenient to read if the cellophane is stiff and dry. The TP swab is soft material which is readily obtained. The direct slide method is not always easy to examine but only a slide is required. The brush method is rather more complicated in preparation and cleaning but is simple to take and is the quickest and simplest for examination for ova. For routine use in survey work, he would recommend either the pestle-slide or the adhesive cellophane (Graham swab) methods, the latter being probably the most convenient for occasional diagnostic use.

REFERENCES

GRAHAM, C. F. (1941) *Amer. J. trop Med.*, 21, 159.
HALL, M. C. (1937) *Amer. J. trop. Med.*, 17, 445.
HELLSTEN, H. (1933) *Nord. med. Tidskr.*, 6, 1358.
NOLAN, M. O., and REARDON, L. (1939) *J. Parasitol.*, 25, 173.
PETERSEN, M. C., and FAHEY, J. (1945) *J. Lab. clin. Med.*, 30 (3), 259.
SCHUFFNER, W., and SWELLENGREBEL, N. H. (1943) *Zbl. Bakt.*, 151, 71.
—— —— (1944) *Zbl. Bakt.*, 151, 114.
WATSON, J. M., and MAC KEITH, R. C. (1946) *Trans. R. Soc. trop. Med. Hyg.*, 40 (4), 376.

[*March* 28, 1947]

DISCUSSION ON ANÆSTHESIA IN CHILDREN

Dr. R. W. Cope: In this Discussion we shall consider the principles rather than the details of technique underlying children's anæsthesia.

Apart from the difference in size of the actual apparatus and dosage of drugs used, how does this anæsthesia differ from that of adults? The reason for considering these differences lies in the fact that a bad anæsthetic will kill a child far quicker than it may kill an adult. A small degree of respiratory obstruction will rapidly change a normal, healthy baby to one who is grey, does not breathe at all, whose pupils are beginning to dilate and whose life is slipping quickly away.

The normal metabolic rate.—This is of importance throughout every moment of a child's anæsthesia. In the human subject the curve of oxygen demand and reflex irritability are parallel. The normal child therefore between the ages of 2 and 12 years will tolerate larger amounts of anæsthetic than might be expected for the size of the patient. A further point in this connexion is that the most frequent factor in producing a temporary rise in metabolism is apprehension and fear. Herein lies the great value to the anæsthetist—quite apart from the inestimable value to the parent and child—in the pre-operative administration of the barbiturates. By allaying fear and inducing normal sleep they are effective in lowering the increased metabolism. Since 1938 it has been the routine practice to use one of the barbiturates, either nembutal or seconal, before most operations at Great Ormond Street Hospital. To deprive a child unnecessarily of the benefit of this simple medication must help to put Medicine back many years.

the tube tends to slip upwards (i.e. anteriorly) into the glottis rather than downwards. Alternatively a stilette may be used in the tube and the tip tilted slightly upwards.

And here I should like to urge the abandonment of that prevalent practice among anæsthetists of using the right hand for introducing the laryngoscope, and having exposed the cords, changing over to the left, which is at best an awkward and inefficient piece of technique.

Having passed the tube and connected up to the apparatus, the first act of the surgeon after draping the child is to secure the endotracheal tube by stitching it to the tongue. This is done because the child is being carried at a very light stage of anæsthesia and is able to gag the tube out of the glottis. Furthermore, the surgeon may inadvertently withdraw the tube whilst changing a throat pack. I have seen both these accidents.

Now to consider the actual anæsthetic.

Premedication consists of atropine only.

Induction is with gas and oxygen and here great care must be exercised. The margin between consciousness and anæsthesia is a very narrow one and whereas at one moment you have a lustily crying baby, the next you may be faced with a deeply cyanosed, limp child who makes no effort at voluntary respiration and who is very near death. Having induced the child, ether is added until anæsthesia is deep enough to enable a tube to be introduced. I never use a throat spray which I consider superfluous. From now on the child is run on gas and oxygen. I find 20% oxygen sufficient and this proportion can be reduced with safety if necessary. The ordinary expiratory valve is used (fully open, of course), there being no necessity for an open outlet to the air. These children remain a good colour and respiration is as a general rule quiet and unhurried. With this rather high percentage of oxygen anæsthesia tends to lighten and usually drops to the second stage. Yet in spite of the light plane of anæsthesia, the absence of sedative premedication and the avoidance of a throat spray, these children tolerate the presence of a tracheal tube without coughing or straining. Nor does sickness occur either during or after the operation. When at the end of the operation the tube is finally removed, the child is fully awake and crying within a minute or so, apparently none the worse for its recent ordeal.

The operation for cleft palate is carried out in children at the age of about eighteen months. Nasal intubation is used in these cases and once again the tube is a problem. The Magill tube tends to kink just inside the nostril where it fits on to the metal connecting piece. The Woodfield-Davies tube has a collar and flange fitted to its proximal end and effectively overcomes this trouble by reason of the collar which reinforces the tube at its vulnerable point.

Regarding blind intubation, generally speaking the younger the child the less likely you are to succeed. Before abandoning this method it is worth while placing the fingers of the left hand under the neck and exerting a firm upward pressure at the moment of pushing the tube on. This manœuvre will often cause the tube to slip into the glottis. Incidentally it is frequently successful in the case of adults. If it is necessary to resort to the laryngoscope, a fine pair of crocodile forceps is preferable to Magill's laryngeal forceps which are somewhat bulky in this small space.

The anæsthetic for these cases is very similar to that for hare-lip.

In view, however, of the constant swabbing and sucking out of the pharynx excessive gagging often becomes troublesome to the surgeon and it is usually necessary to add at intervals small amounts of ether. But this is never sufficient to cause abolition of this reflex by the time the operation is over, since the surgeon is anxious at this point to test the child's ability to close the pharynx following his handiwork. When diathermy is used trilene is given instead of ether, but I find these children remain drowsy, sometimes for long periods, and do not recover so well as the others.

sprung's disease. The condition of congenital hydro-ureter has been investigated by spinal analgesia. What neurological imbalance is present here? And, if there is imbalance, what help can anæsthesia give? Scholefield and Chivers (1947) have recently published a report of the results of injecting the splanchnic ganglia with weak amethocaine solution in 5 cases of congenital megacolon. The results were encouraging, and it is hoped to repeat their work shortly.

REFERENCES

COURT, D., and HASLER, J. K. (1942) *Proc. R. Soc. Med.*, 35, 687.
HAWKSLEY, M. (1943) *Proc. R. Soc. Med.*, 36, 586.
—— (1944) *Brit. J. Surg.*, 31, 245.
SCHOLEFIELD, J., and CHIVERS, E. (1947) *Brit. J. Anæs.*, 20, 3.
TELFORD, E. D. (1939) *Proc. R. Soc. Med.*, 32, 1145.

Dr. D. Aserman: *Anæsthesia for hare-lip and cleft palate.*—The operation for hare-lip is performed on children of about three months. An infant of this age requires a No. 0 or No. 1 size endotracheal tube which is passed through the mouth. The ordinary Magill tubes in these sizes are too thin and flimsy to be safe, since, however carefully they are connected up, there is a considerable risk of kinking.

To overcome this difficulty Mr. Humby and I evolved at the beginning of the war the Humby Tube which I continued to use for some considerable time. But this tube was designed primarily for use with the Davis gag which held the tube snugly and firmly in position and assured a correct alignment of the rubber end-piece. In the absence of the Davis gag, however, the fitment tends to ride upward in the mouth, occasionally causing a slight bending of the rubber tube at its junction with the metal and thereby a certain measure of respiratory obstruction.

Mr. Denis Browne's solution of this problem consists of a reinforced tube—an ordinary Magill tube cemented within a tube of larger bore, the inner tube being prolonged beyond the outer to the extent of an inch and a half or so. This tube can be bent to almost any angle without kinking; it is simple and inexpensive and I now use it for all oral endotracheal work in children with complete satisfaction.

(I must point out that, although the first tube I saw was that of a rough model made by Mr. Denis Browne, yet apparently Dr. Magill had produced an identical tube a good many years previously.)

Two other tubes should be mentioned in this connexion. The Magill armoured tube is excellent, but it is expensive, delicate in structure and easily damaged. Portex tubes tend to soften as they warm up to body temperature and, at any rate in the sizes under discussion, they are not safe.

Turning now to the actual introduction of the tube, this little operation in the case of hare-lip can be extremely difficult. In the choice of laryngoscope my own preference is for the Magill and I invariably use the adult size blade, even in the case of the smallest infants. This gives that extra amount of room which can be so helpful. I am equally at ease with the right-angled or Guedl-angled patterns. In the case of hare-lip associated with cleft palate, on introducing the laryngoscope the edge of the blade is liable to slip into the cleft and one free end of the alveolus may drop into its lumen. When this occurs it is usually impossible to pass a tube through the restricted space and I know of no cases more difficult to intubate than these. Mr. Denis Browne has designed a special spatula to deal with this problem. This is somewhat similar to a Magill but is much broader at its proximal end and this extra width is intended to bridge the gap in the alveolus. I, personally, prefer manœuvring the ordinary spatula into position, usually by introducing it well over to one side.

It is in many cases impossible to expose the cords fully and only the posterior portion of the glottis can be seen. On attempting intubation in this situation the tube often refuses to enter the glottis and slides downwards off its posterior aspect. This can be overcome by recutting the end of the tube so as to bring the chamfer to its lower aspect, whereas it normally lies to the left. It will now be found that

Urine: Acid, alb. 1,600 mg.%. Deposit—a few W.B.C., R.B.C. and casts. Blood urea 38 mg.%. Serum protein 3·9%.

Put on to high protein salt-free diet. Total 82 grammes protein per day. Œdema rapidly subsided and clinical condition improved.

28.3.47: Plasma—Fibrin 0·48%, alb. 2·18%, glob. 1·83% (total 4·49%). Blood cholesterol 408 mg.%.

2.4.47: 2 grammes NaCl added to diet. Œdema immediately increased, marked rise in weight.

8.4.47: Diet salt-free again, weight remained stationary.

10.4.47: 2 grammes KCl added to diet followed by fall in weight.

Hypoplastic Anæmia.—I. A. B. CATHIE, M.D.

E. J. B., female. Normal birth (28.3.45). No neonatal jaundice.

Family history not significant.

History.—Pallor since birth; at 3 months Hb 24%, rose to 80% after transfusion but within a month had fallen to 49%. Further transfusions given. At 3 months passed bright blood in stool once. At 4 months purulent right ear discharge.

Admitted 29.9.45, aged 6 months. Well-nourished. Slight icteric tint to sclerotics. Liver enlarged 1 in. and spleen 1½ in. Right ear discharging.

Investigations.—Blood-count: R.B.C. 1,330,000, Hb 30% (4·2 grammes), C.I. 1·1. W.B.C. 17,700 (lymphos. 54%, poly. neutros. 44%, eosinos. 2%). Reticulocytes 0·2%, normoblasts 2 per 100 W.B.C. M.C.D., M.C.V. and M.C.H.C. within normal limits. Platelets 350,000. Red cell fragility normal. Cold agglutinin titre 1 : 4 at 8° C. W.R. and Kahn negative. Blood cholesterol 95 mg. per 100 c.c. Blood phosphatase 14 units. Takata-Ara reaction negative. Serum bilirubin 2·5 mg. per 100 c.c. Histamine test meal showed hypochlorhydria. Mantoux negative. X-ray chest and long bones—no abnormality. Bone-marrow (*see below*).

Progress: Since first admission, transfusions given about every six weeks, but Hb level falls steadily in intervening periods. Numerous forms of therapy have been tried, including iron, liver extract, proteolysed liver, vitamin B, ascorbic acid, thyroxin, penicillin, sulphonamides and bilateral mastoidectomy, without success.

Present condition: Aged 2 years, weight 28 lb. Does not walk. Readmitted 28.3.47 with bronchopneumonia and purulent discharges left eye and left ear. Liver 2½ fingerbreadths below costal margin. Spleen much enlarged.

Blood-count: R.B.C. 3,200,000, Hb 65% (9·1 grammes). W.B.C. 19,300 (polys. 73%, lymphos. 27%). 1.4.47: Transfusion of 1 pint. Hb next day was 100% (14·0 grammes). On 8.4.47 reticulocytes less than 0·1%. 10.4.47: Folic acid 15 mg. daily (intramuscularly).

SERIAL BONE-MARROW COUNTS

	1945			1946				1947
Date:	4.10	31.10	14.11	9.1	1.2	9.3	30.10	9.4
Premyelocytes	—	—	—	—	3	1	1	1
Myelocytes	3	10	1	1	2	2	1	4
Metamyelocytes ..	1	5	2	5	18	10	6	16
Stab forms	23	14	10	3	5	9	7	36
Polymorphs	6	15	10	4	5	7	4	12
Lymphocytes	18	27	55	72	43	49	67	22
Monocytes	—	—	—	—	2	1	1	—
Hæmocytoblasts ..	1	—	—	1	—	—	—	0·1
Erythroblasts	3	10	5	8	6	1	—	1
Early normoblasts ..	1	12	10	3	7	5	2	2
Late normoblasts ..	44	7	7	3	9	15	11	6
Myeloid/red ratio ..	1 : 1·5	1·5 : 1	1 : 1	1 : 1·1	1·5 : 1	1·4 : 1	1·5 : 1	8 : 1

Dr. I. W. Magill said that children do not stand suboxygenation well. He had abandoned nitrous oxide in favour of ether for dissection of tonsils and was convinced that results were better with this agent. In premedication, he was surprised that more use had not been made of opiates in suitable doses since such drugs were indicated where the metabolic rate was high, as it usually is in children.

Endotracheal tubes of rubber composition were made by different manufacturers and varied much in consistency. It was the duty of the anæsthetist to see that the tube was satisfactory before using it. For hare-lip and cleft palate operations in infants he had experimented with tubes of gum elastic, metal, and rubber composition, including tubes of different calibre cemented together. He had found an armoured tube satisfactory. The anæsthetic was delivered directly into the funnel-shaped outer end by a side inlet. There was no rebreathing. A useful protection for this tube was a small gutter made of malleable metal applied at the point where the tube rested on the alveolus.

[*April* 18, 1947]

MEETING HELD AT THE HOSPITAL FOR SICK CHILDREN, GREAT ORMOND STREET, LONDON, W.C.1

Diabetes Insipidus.—B. W. POWELL, M.B., M.R.C.P. (for BERNARD SCHLESINGER, F.R.C.P.).

G. L., boy aged 1 year; failed to thrive since 4 months. Thirst since birth.

Family History.—First pregnancy. Father's father and two brothers have diabetes mellitus.

History of present illness.—Since 4 months old has had bouts of vomiting lasting two to three days, coming on at intervals of several weeks. Has always been very thirsty and now gets three to four pints in a day. Has always been constipated.

On admission: Weight 14 lb. 10 oz., height 26·5 in. A wasted baby but with good hydration clinically. Liver edge palpable and tip of spleen just felt. Mantoux 1 : 1,000 negative. X-ray skull normal.

Blood-count: R.B.C. 4,400,000, W.B.C. 18,500.

Blood chemistry—28.3.47: Urea 53, chlorides 852, protein 7·4.

31.3.47: Urea 42, chlorides 637, protein 6·8, bicarb. 57 vols.%.

8.4.47: Urea clearance 81% of normal. Blood urea 40.

9.4.47: Total volume urine excreted 37 oz. S.G. 1002 (intake 50 oz.).

In view of normal kidney function and continued polyuria and thirst, is thought to be a case of diabetes insipidus.

Nephritis with Œdema.—B. W. POWELL, M.B., M.R.C.P. (for BERNARD SCHLESINGER, F.R.C.P.).

B. W., boy aged 3 years.

6.3.47: Loss of appetite, pale stools, dark urine (mild hepatitis).

9.3.47: Urine became scanty and œdema developed. No albuminuria at this time. Improved on high protein diet but after a few days œdema increased again and abdomen became swollen.

12.3.47: Seen as out-patient. Some œdema. No albuminuria. Blood urea 27 mg.% Plasma proteins: Fibrin 0·4%, albumin 1·36%, globulin 1·83% (total 3·59%), alb./glob. 0·75 : 1.

20.3.47: Admitted to hospital. Gross œdema. Tonsils large. Heart: Apex beat 5th space anterior axillary line. B.P. 115/70. Fundi normal. Abdomen: Some ascites.

erythroblastæmia were recorded as important features. Next, interest shifted to the pathology, studied and fully described by German investigators, between 1910 and 1920. Finally, the anæmia developing unexplainably in newborn infants was considered a new entity, shortly after 1920.

Our own interest in and experience with erythroblastosis fœtalis dates back twenty years, and in 1932 we collected and published records of 20 infants, suffering from œdema at birth, or jaundice and anæmia shortly after birth, splenomegaly and erythroblastæmia—all being manifestations of a single underlying morbid process.

The discovery of the Rhesus blood factor in humans in 1940 and in 1941, its important relation to erythroblastosis fœtalis, once more focused attention on this disease. In the succeeding five years, so much has been written on the Rh factor, and the disturbances which result from it, that it is worth while reviewing the subject and considering what is established fact and what is hypothesis.

The Rh blood factor is present in the red cells of 85% of the white population and absent in 15%. Since it is foreign to the system of the latter group, the Rh factor can act antigenically to start isoimmunization, when introduced into the body, either by transfusion or, in women—and even then only in a small percentage of them—by pregnancy. The antibodies produced by the Rh-negative individual, after sensitization, are agglutinins, capable of clumping and eventually destroying Rh-positive red cells. It usually requires one or more transfusions of Rh-positive blood into an Rh-negative patient, and an interval of two weeks or more, before a hæmolytic reaction is produced.

In women, subject to sensitization via pregnancy, even a first transfusion of Rh-positive blood may cause a serious untoward reaction. The factors which govern this are, first, the combination of an Rh-negative mother and an Rh-positive father, to whom are born Rh-positive children. These may serve to sensitize the woman when fœtal erythrocytes or tissues enter her circulation during gestation. Thereafter, the transfusion of this Rh-negative woman with Rh-positive blood will lead to a hæmolytic crisis.

Actually the danger of isoimmunization of the Rh-negative woman by pregnancies involving an Rh-positive fœtus is relatively small, since about 13% of all marriages are between an Rh-negative woman and an Rh-positive man, but only 1 in 150 deliveries produces an infant with erythroblastosis fœtalis, and even so the first Rh-positive infant almost always escapes. This means that less than one such woman in twenty need be concerned about becoming sensitized through pregnancy alone. However, a single transfusion of Rh-positive blood, followed by pregnancies, will increase the chances of trouble from 5% to over 50%.

Another hazard of isoimmunization following transfusion affects the fœtus. If an Rh-negative woman is given Rh-positive blood, the antibodies which develop may produce hæmolytic disease in any subsequent Rh-positive fœtus, even if it is a firstborn.

The modes of Rh sensitization of the Rh-negative woman then are, first, through transfusion of Rh-positive blood, second, through repeated pregnancies with Rh-positive babies, and third—a little appreciated menace—through the injection intramuscularly of even small amounts of Rh-positive blood, a mode of therapy fortunately now discarded for the treatment of hæmorrhagic diseases, pernicious vomiting of pregnancy and stubborn dermatitis. Although such intramuscular blood probably does little or no harm alone, if followed by Rh-positive pregnancies, even years later, it may be important in initiating isoimmunization.

The woman who, through any of the above mechanisms, has become sensitized against the Rh factor, may face several serious problems in subsequent child-bearing. If she is fortunate enough to marry an Rh-negative man—about one chance in seven—she need have no fears, since Rh-negative children will not be affected. If the sensi-

Sturge-Weber Syndrome.—N. F. ELLIOTT BURROWS, B.M. (for W. G. WYLLIE, M.D.).

A. McK., aged 1 year. Born with capillary angioma over entire left side of face and scalp. History of frequent twitchings, and turning of the eyes generally to the right. Pneumo-encephalography revealed a gross defect inside the skull on the side corresponding to the angioma.

Dr. F. Parkes Weber considered the diagnosis completely proved. The typical calcification would probably develop later. In regard to the relative parts played by Dr. W. Allen Sturge (1879), the pathologist, Dr. S. Kalischer (1901), and others, in the discovery of the syndrome, *see* F. P. Weber, *Rare Diseases and Some Debatable Subjects*, second edition, London, 1947, p. 9.

Dr. Parkes Weber continued: The condition is obviously a result of dysplastic development (partly definitely "hamartomatous") of the vascular elements of the affected portions of the skin and lepto-meninges (with underlying surface of the cerebral cortex). Sometimes there is congenital glaucoma (buphthalmus) on the same side as the cerebral lesion—evidently of analogous dysplastic origin. Apart from a possible inborn tendency in some families to dysplastic and hamartomatous development of various kinds, the condition seems not to be hereditary, but seems more likely due to some local accident of unknown causation, affecting the embryo during early intra-uterine life. Cases of the syndrome are by no means so rare as was formerly supposed.

Exophthalmic Goitre.—J. M. ALEXANDER, M.R.A.C.P. (for W. G. WYLLIE, M.D.).

J. L., aged 9 years, the second child of nervous parents, started having night terrors about 6 months before admission, when eyes became protuberant and pulse very fast. Also had profuse sweats.

On admission: Enlargement of thyroid gland, and fibrillary tremor of outstretched hands.

POSTSCRIPT (22.7.47).—Thyroidectomy has been performed. Symptoms have disappeared and eyes now appear normal.

Neurofibromatosis.—J. M. ALEXANDER, M.R.A.C.P. (for W. G. WYLLIE, M.D.).

M. B., aged 10 years, only child of healthy parents, born with two café-au-lait spots on buttocks and one on chest.

In 1941 had a fall; left shoulder became swollen two weeks later; glandular swelling in this region. Biopsy: Neurofibromatotic tissue. Given deep X-ray treatment, but three months later egg-shaped swelling underneath outer part of left clavicle reappeared. Café-au-lait spots increasing in number.

Pseudo-hypertrophic Muscular Dystrophy.—J. M. ALEXANDER, M.R.A.C.P. (for W. G. WYLLIE, M.D.).

G. Y., aged 5 years, has had difficulty in walking, particularly upstairs, for three years. "Climbs up himself".

Weakness of proximal muscles of legs and hypertrophy of calves.

[*May* 23, 1947]

Erythroblastosis Fœtalis or Hæmolytic Disease of the Newborn

(*Abstract of Illustrated Talk*)

By LOUIS K. DIAMOND, M.D.

(*The Children's and Infants' Hospitals, and Harvard Medical School, Boston, Mass.*)

RECENT and more widespread interest in erythroblastosis fœtalis or hæmolytic disease of the newborn has led to the erroneous impression that this is a new condition of recent origin. Actually it was well described, in the English literature, before 1900, being then recognized in the form of fœtal hydrops. Between 1900 and 1910, there were numerous articles, published in this country, dealing with familial icterus gravis, another manifestation of the same disease, and even the severe anæmia and

and fortunately did not recover. If they did improve, marked developmental retardation and muscle unbalance might result. Pathologically, kernicterus was usually found in such patients. This is a diffuse and symmetrical staining of nerve cells. It is unrelated to simple mechanisms such as intravascular thrombi or agglutination of red cells.

The tendency for the recurrence of infants with erythroblastosis fœtalis was always disturbing, especially since the disease became progressively more severe in succeeding siblings. Often, this resulted in the birth of hydropic stillborns, with severe anæmia, tremendous splenomegaly, hepatomegaly, and dilated hearts. Then again, a single child might escape serious damage and exhibit only moderate and easily repaired anæmia.

Not all of these clinical observations have been explained by the discovery of the Rh factor and the knowledge of the action of anti-Rh agglutinin on the Rh-positive infant's red cells. The serologists have tended to oversimplify the pathogenesis of the disease and draw too many analogies between what happens in the baby and what can be demonstrated in the test-tube.

With the disclosure of the role of maternal Rh antibodies in damaging the infant's Rh-positive red cells, it seemed logical to use only compatible Rh-negative blood for transfusion of the anæmic infant with erythroblastosis fœtalis. Such transfusions were given as frequently as needed, always into an easily accessible superficial vein, in amounts of about 10 c.c. per pound of body-weight, using a pressure system. More may be given, but if the infant has cardiac dilatation or a tendency to develop petechial hæmorrhage, sudden collapse may occur during large transfusions from cardiac decompensation or diffuse hæmorrhage.

During a period of about three years when our treatment consisted only of repeated small transfusions of Rh-negative blood, the gross mortality from erythroblastosis fœtalis seen in our clinic was about 30%. This improvement may have been due to earlier recognition and treatment of such infants as well as the use of Rh-negative blood transfusion.

By 1944, most of the obstetricians were well aware of the dangers of Rh antibodies in Rh-negative women, and were testing such patients more regularly. We had organized several prenatal clinics for the care of these problems and were following the titres in sensitized women throughout pregnancy. It was always distressing to detect a rising or a high titre, to wait for the delivery of the infant at term, and to have the infant succumb *in utero* only a few weeks from term, or even shortly after birth. In such cases, it seemed reasonable therefore to try to deliver the sensitized woman two or three weeks before term. During the years that this has been practised in conjunction with frequent transfusions of Rh-negative blood, as needed, the gross mortality has been lowered to 20%.

Finally, another improvement in therapy was attempted. We had shown for some time that the erythroblastotic infants who were most seriously ill or suddenly collapsed after being quite normal in appearance at birth, usually showed free maternal antibody in their cord blood. It seemed likely that this continued acting in the child's system and caused the sudden change for the worse in succeeding days. In addition, many of the babies' red cells were proved to be coated with maternal antibody. The removal of as much as possible of the affected infant's circulating blood, shortly after birth, in proper cases, seemed desirable.

The first attempts to do an early exsanguination-transfusion were complicated by mechanical difficulties. The longitudinal sinus is a dangerous vessel to puncture blindly, particularly in a newborn infant, whose head is moulded out of shape with normal anatomic relations distorted. Peripheral veins are small and fragile. Even arteries may be too small for ready cannulization and the exposure of a sick newborn infant for an hour or two while vessels are exposed and used may be a cooling and tized woman has an Rh-positive husband who is homozygous, i.e. carries two Rh-positive genes, every infant will be Rh-positive and will be affected, usually with increase in severity of the disease. If the husband is heterozygous, Rh-negative children are possible and only the Rh-positive infants may have erythroblastosis fœtalis.

It is important, therefore, not only to determine the Rh type of every recipient of blood and every woman during child-bearing, but if Rh sensitization is detected in the woman, to test the husband's blood for homozygosity or heterozygosity and so be able to prognosticate the chances of successful pregnancy. For such special tests, the ordinary simple Rh-typing serum must be supplemented with special specific anti-Rh serums which can only be found in certain diagnostic laboratories.

Prior to 1944, tests for sensitization of Rh-negative individuals were often quite unsatisfactory since, even in instances of proven hæmolytic transfusion reaction or definite erythroblastosis fœtalis, the serum of the affected individual often failed to disclose Rh agglutinins. In 1944, new tests were developed which detected antibodies coating Rh-positive red cells or blocking their further agglutination in saline suspension, or clumping them only in protein media. These new and more complex antibodies were named "incomplete antibodies", "blocking antibodies" or "hyperimmune antibodies". The latter name arose from the finding that if human experimental subjects were injected repeatedly with Rh-positive blood cells, their serum first contained ordinary agglutinins acting against Rh-positive red cells suspended in saline. These were named "early antibodies". With continued injections, such Rh-negative persons gradually lost their simple Rh agglutinins, but developed the "incomplete" or "blocking" form which no longer agglutinated Rh-positive cells in saline but did become attached to such cells and could clump them in plasma, serum, or albuminous suspension media, and, of course, did produce agglutination within the body. These were named "hyperimmune antibodies". They are more complex, much more stable and long-lasting and probably can produce more damage, especially to Rh-positive infants developing erythroblastosis fœtalis.

Just as in these experimental subjects stimulated by blood injections, Rh-negative women bearing Rh-positive infants, tend first to develop early saline-acting agglutinins but with succeeding pregnancies, form more of the hyperimmune antibodies and, later, only this form. However, the form of Rh antibody and its concentration or titre bear no direct relation to the severity or the type of erythroblastosis fœtalis which develops in the child of the sensitized woman.

Certainly only the roughest parallelism is to be found between the type of Rh antibody and its amount during and after pregnancy, and the form of the disease or its severity in any given infant. In general, the hyperimmune and high titred Rh antibodies are found in association with the more serious or more often fatal types of hæmolytic disease in the newborn. But a prognosis based on antibody tests and titres, in any given case, must be offered with reservations.

With regard to the clinical problems faced by the pædiatrician or practitioner, our own experience began about twenty years ago, when we first treated newborn infants with jaundice and anæmia, using compatible blood from the father (therefore Rh-positive) for transfusion. Many transfusions were often necessary since the red cells did not seem to survive long, but eventually a majority of such children recovered, especially if they had no complications such as severe jaundice, œdema, diffuse hæmorrhage or cardiac failure with secondary pneumonia. Over a period of fifteen years, including the infants who were born dead and diagnosed by the pathologist, we found a gross mortality of about 40%. Several features were intriguing then, just as they are now. Often, newborn infants displayed very little anæmia, but developed early and severe jaundice. Transfusion did not materially benefit these and sometimes they developed signs of brain damage, about the fourth or fifth day of life,

Section of Neurology

President—DOUGLAS MCALPINE, M.D., F.R.C.P.

[*February* 6, 1947]

CLINICAL MEETING HELD AT NATIONAL HOSPITAL, QUEEN SQUARE, LONDON

Dystonia Musculorum Deformans with Another Case in the Same Family.—DIANA BECK, F.R.C.S.

A. S., a schoolgirl, aged 8½ years, regarded as hysterical, but was referred to the Neurosurgical Unit from an orthopædic clinic for exclusion of organic disease.

The child of a normal, full-term first pregnancy terminated by a normal delivery without birth injury, the patient was perfectly well until a year ago when she began to kick up her left heel on walking. This was shortly followed by a similar uncontrollable disability on the right side; within six months she could only walk with support. Fine tremor of the hands had been observed throughout the illness.

The family history is of interest for the child's paternal uncle, L. S., now aged 39, began to have difficulty in walking at the age of 8 and with the years became progressively more unsteady. His disorder was diagnosed as chorea. He has never worked on account of his disability.

L. S. is an intelligent and otherwise healthy man. Spasmodic contractions of the masseters. Both sternomastoids contracted with periodic spasm; intermittent backward jerking of the head. Roving movements of the tongue. All limbs in continuous state of tremor and tension; rhythmic twitchings of biceps and triceps. Power in upper limbs good: impairment in lower limbs owing to severe spasm, especially marked in adductors and glutei. Great difficulty in walking: legs crossed; both feet in position of talipes equino-varus. No sensory or reflex disturbance.

The patient is a pale, auburn-haired little girl with a somewhat expressionless face. Very intelligent (I.Q. 148); emotionally mature and well balanced.

General examination normal. Cranial nerves normal. Roving movements of the tongue. Fine tremor of head and trunk, especially marked on standing up. Fine tremor of hands at rest; athetoid movements of outstretched arms; constant opening and closing movements of hands. There is diminished tone in the arms after initial difficulty in relaxation has been overcome; tone is increased in the lower limbs; both heels drawn up. No ataxia; no inco-ordination; no motor weakness. Fine movements somewhat clumsy. Stands and walks with hips and knees flexed; there is adduction and internal rotation at the hip-joints and the heels are drawn up whilst the feet are inverted. Gait very unsteady and only possible with support. Scoliosis with convexity to the right. Sensation normal. Tendon reflexes present and equal but difficult to elicit. Abdominal reflexes present and equal. Plantar reflexes flexor.

Investigations.—X-rays of skull and spine normal. Cerebrospinal fluid: clear, colourless: protein 25 mg.%; no cells; sugar 54 mg.%; chlorides 750 mg.%. Blood and cerebrospinal fluid: Wassermann negative. Liver function tests: Serum alkaline phosphatase 14 units; thymol turbidity 3 units; plasma proteins:—Total 5·9% = albumin 2·6%, globulin 3·02%, fibrinogen 0·28%, A/G ratio 1 : 1·2.

Electro-encephalogram.—Delta and theta discharge larger in postcentral regions and often focal on left side; almost completely inhibited on opening eyes. Frontal regions: strikingly little electrical activity. Electrical activity from central and postcentral structures closely resembles records from normal children of 1½ to 3 years. Tracings from precentral areas normal for child's age.

Electromyogram.—(*a*) Surface electrodes: motor unit discharge from both flexors and extensors. Relaxation slow. (*b*) Needle electrodes: some motor unit action potentials firing synchronously.

shock-producing procedure. Needles and tubing tend to clog as the blood thickens or the flow slows. The injection of heparin to prevent clotting is a decided risk in an infant who usually has hypoprothrombinæmia and a well-marked bleeding tendency.

Only through the development of special plastic catheters and their use in the umbilical vein were all these difficulties resolved and the techniques of exsanguination-transfusion made easier.

The indications for this operation have been fixed as follows until such time as sufficient data have been accumulated to evaluate the results. If the mother has been known, or is quickly demonstrated, to have Rh antibodies in her serum, and the infant shows definite clinical signs of erythroblastosis fœtalis, at or shortly after birth, treatment is begun at once. If the infant born to a sensitized mother exhibits no symptoms at birth, but is found, by immediate testing of the cord blood, to be Rh-positive and to have detectable Rh antibody still present in its serum, treatment is also indicated. If the infant not only looks well, but though Rh-positive has no free maternal antibody by suitable tests, no treatment is given at present. To date, about ten such infants have had no serious anæmia later, although a few of them have required single transfusion.

The results of exsanguination-transfusion have been quite satisfactory in many cases. Infants, very sick and anæmic at birth, have survived. Most of them have been ready for discharge with the mother in seven or eight days. Only a few have developed moderate anæmia by the third week and required another small transfusion.

Statistically, our mortality in about fifty sick infants has been near 10%. Several babies who succumbed had atelectasis, intracranial hæmorrhage and other signs of immaturity, rather than erythroblastosis fœtalis.

Much more study and data are needed before the problems of the management of blood incompatibility—antibody action between mother and child—and the best care of the newborn infant with hæmolytic disease are all solved. Notable advances have been made. But there is no justification for complacency or surety. Neither is there reason for undue anxiety when faced with the problems of Rh incompatibility.

[*June* 14, 1947]

MEETING HELD AT ROYAL VICTORIA INFIRMARY, NEWCASTLE-UPON-TYNE

The following papers were read:

Problems in the Organization of a Professorial Unit.—Professor J. C. SPENCE, M.C., M.D.

A Method of Recording Neonatal Infections in a Maternity Hospital.—MARY TAYLOR, M.D.

Prematurity in an Industrial Town.—F. J. W. MILLER, M.D.

Treatment and Prognosis of Bronchiectasis.—ALAN OGILVIE, M.D., F.R.C.P.

A Consideration of Acute Intussusception in relation to Medical Teaching.— DONALD COURT, M.R.C.P.

There were enlarged glands in the groins and right axilla; spleen palpable.

Dr. Macdonald Critchley showed radiographs indicating a condition of osteitis and periosteitis of the right femur. X-rays of the chest showed a soft swelling over the ribs on the right side which he imagined represented a gumma. The only other feature of interest was that the man was a eunuch. The most likely explanation of the syphilitic infection was that it was of extragenital origin, though it should be remembered that eunuchs, while not fertile, were not necessarily impotent.

Sir Charles Symonds asked what treatment this case had had. The prognosis in cases of complete spinal block was, on the whole, not a good one. He had had a case, however, of this type treated with penicillin, in which recovery was much more complete than usual.

Dr. Macdonald Critchley said that this patient had had 3·7 million units of penicillin since the onset of the paraplegia, but without effect.

POSTSCRIPT (6.3.47).—Despite another course of penicillin, the patient steadily went downhill and died. Autopsy revealed a condition of lymphosarcoma, with a large mass over the right side of the chest, infiltrating the spinal canal and compressing the cord. The right femur was invested by a diffuse tumour associated with the periosteum. From data subsequently obtained, it seems probable that the lues was of the inherited variety (M. C.).

Myoclonus.—E. A. CARMICHAEL, C.B.E., M.B.

A. L., male, aged 43. Perfectly well until February 1944 when he began to have infrequent generalized epileptiform attacks, sometimes with a focal sensory onset. In September 1944 he experienced progressive difficulty in walking because of involuntary shaking movements of the legs, so that by February 1945 he had to use a stick. By the following September he could only crawl on hands and knees, and by January 1946 he was only able to use his arms to drag himself along the floor.

Since then he has been bedridden. There are increasingly frequent involuntary movements of the limbs and trunk initiated by minimal stimuli, and interspersed by generalized epileptiform convulsions.

There is extreme weakness of the legs, slight weakness of left hand with marked inco-ordination of both arms. Progressive dysarthria and probably mental deterioration also. Nothing relevant in family history or history of past illness.

Dr. E. A. Carmichael said that this case had been the means of demonstrating some interesting central nervous phenomena, which Dr. Dawson had studied.

Dr. G. D. Dawson said that in the investigation of this case the most striking findings were that if any peripheral stimulus was applied it resulted in a very large change of electrical potential over the contralateral scalp. Control experiments showed that this was not an artefact, and that it did represent an electrical change in the brain. The response to stimulation of a leg appeared near the mid-line and to stimulation of an arm 5 to 8 cm. lateral to it. The time between a stimulus and the electrical change showed fairly clearly that the change picked up on the scalp was either associated with the arrival of the afferent volley at the cerebral cortex or occurred very shortly after this. The response occurred some 150 to 200 milliseconds before the myoclonic jerk which Dr. Carmichael had demonstrated. The distribution of the response in an antero-posterior direction was of interest because it was 3 to 5 cm. in front of the surface markings of the central sulcus. In five other cases of myoclonus of comparable severity examined previously, he (Dr. Dawson) had never managed to elicit any response of this sort. This response, then, was unusual and it showed that an afferent volley either had direct access to a much larger number of cortical cells than usual or on arriving at the cortex caused some spreading change there. The methods developed in examining this case had since shown that on peripheral stimulation a similar response could be just detected in the normal, about one-tenth of the size of that appearing in the patient under discussion, and it always appeared over the marking of the central area instead of, as in this patient, farther forward. So far as the secondary jerks were concerned, it seemed possible to suggest that these might be transcortical reflexes, because they were always preceded by the cortical discharges, to which they had a regular time relation. The first stimulus of a series was accompanied by a massive generalized jerking; later stimuli provoked only jerking in the segment stimulated. The cortical response changed in a corresponding manner. The first stimulus provoked a spreading discharge lasting up to a second ; the later stimuli were accompanied by a very much briefer localized discharge.

Dr. Purdon Martin asked whether this patient had pyramidal tract involvement or any indication of cortical atrophy.

Comment.—In the absence of birth trauma, other injury or illness this condition must be ascribed to congenital defect. The points of interest are the family history, the changes in the plasma proteins and the electro-encephalograms. The patient has a diminished plasma protein content and reversal of the albumin-globulin ratio. It might be argued that there is some degree of liver dysfunction in this child; this suggests a link with Wilson's disease. The electro-encephalographic findings are important in view of recent American work in which precentral cortical excisions are undertaken in cases of dystonia musculorum deformans.

Post-encephalitic Parkinsonism with Marked Palilalia.—MACDONALD CRITCHLEY, M.D.

H. S., male, aged 40, sustained an attack of acute epidemic encephalitis in 1924. He made a good recovery until about 1934 when he began to develop drowsiness, and slowness and clumsiness of movements. Another disturbing symptom was a tendency for the eyes to turn up involuntarily (oculogyric crises). On this account he gave up work in 1941. In 1945 his speech showed the repetitive features of palilalia which are now so conspicuous.

Physical examination reveals a Parkinsonian syndrome of moderate severity, more marked on the right side, and with a mild and inconstant degree of tremor.

Dr. Critchley added that there were a number of interesting neuro-psychiatric features in this case. One was his tendency to compulsive thinking, especially during the oculogyric crises, but at other times also. He would be compelled to repeat to himself a number of rhymes or verses of poetry. He was also apt to identify himself in the cinema with the characters on the screen and this feeling would persist for a while even after leaving the theatre. A third feature of his case, which is now a thing of the past, was the occurrence of bouts of rapid noisy breathing. The outstanding characteristic at present is his palilalia whereby he repeats the last few words of a sentence over and over again—perhaps as many as 15 times. But if requested to narrate a preformed speech pattern (days of week, &c.) or to recite something he knew by heart, no palilalia would occur.

A final interesting feature is his tendency to continue unduly any repetitive act, such as hammering a nail, combing his hair, or brushing his teeth. Whether this movement-perseveration represents a real palipraxia, or whether his involuntary tremor in such circumstances takes control of his volitional movement, is uncertain. His tremor, however, was 5·5 per second and his movement repetitions were much slower and were perhaps on that account to be regarded as a true psychomotor disorder, or a palipraxia.

In reply to Sir Charles Symonds, who asked whether the patient still got his oculogyric crises, which on the whole carried a better prognosis than any of the other symptoms, Dr. Critchley said that though much less frequent than formerly he did not think they had entirely disappeared. His experience too was that these oculogyric crises, unlike the Parkinsonian syndrome, were features that improved.

The President asked about the psychological background of the patient, to which Dr. Critchley replied that the man's personality prior to his illness was not of the obsessional type.

Paraplegic Eunuch with Lues.—MACDONALD CRITCHLEY, M.D.

D. F., male, aged 46, entered hospital at the end of November 1946 on account of pains in the right side of the chest and in the right leg. Whilst under observation he developed numbness over the abdomen, and later, a total flaccid paraplegia with incontinence and loss of sensation up to the level Th. 6. Lumbar puncture: yellow fluid; Queckenstedt positive; 18 cells, protein 180 mg.%. W.R. and Kahn positive in fluid, negative in blood.

The patient was 6 ft. 2 in. in height, with long slender extremities, smooth hairless skin, small penis and testes, no beard, pubic or axillary hair, high-pitched voice.

carotid ligature was considered inadvisable. He hoped that Dr. Meadows would publish the cases he was collecting since the correct treatment for this somewhat rare condition was still in doubt.

Dr. Purdon Martin had seen two cases in which there had been a thrombosis of the cavernous sinus after rupture had occurred. One of them came to post-mortem later and it was possible to confirm the diagnosis. The other patient lost all ocular movements and became blind; about a week later he recovered and was said to have left hospital quite well. Recovery was certainly possible.

Dr. Meadows, in reply to Dr. Purdon Martin, who asked whether any good was done to this patient by tying her carotid, said that before operation the proptosis was increasing considerably, and she was complaining bitterly of the bruit. Now she was very much better, the exophthalmos had almost disappeared, and the faint bruit did not trouble her.

Papillœdema associated with Chronic Bronchitis, Emphysema and Polycythæmia.—S. P. MEADOWS, M.D.

D. G. R., male, aged 42. Chief complaint is that of insomnia for past few years, due to bronchitis. Recurrent bronchitis with asthmatic attacks for over twenty years, worse during the winter. Dyspnœa on exertion past few years. Morning headaches when he sleeps badly.

On examination.—Obese, plethoric, cyanosed man. Moderate dyspnœa on exertion. No finger clubbing. Bilateral papillœdema with hæmorrhages scattered about the retinæ. V.A. 6/9. Visual fields full. No other abnormal signs in C.N.S. Lumbar puncture: C.S.F. pressure 240 mm. C.S.F. normal. Chest: Poor expansion, poor air entry with expiratory wheezings. Heart clinically normal. B.P. 140/80. No congestive failure. E.C.G.: Right ventricular preponderance. He had a short attack of auricular fibrillation while in hospital in December 1946.

Ventriculogram: Normal ventricular system. X-rays: Skull normal. Chest: Well-marked emphysema with very poor expansion of lungs and practically no diaphragmatic movements. Slight cardiac enlargement, both right and left ventricles. Main pulmonary artery and its branches are dense. The appearances may be due to pulmonary arteriosclerosis. Vital capacity: 1,562 c.c. (about 1/3 normal). Renal function tests normal.

Blood-count: Shows polycythæmia. R.B.C. 8·22 million and 6·82 million on different occasions, with 134% and 116% hæmoglobin.

Dr. Meadows suggested that the papillœdema in this case was secondary to the chronic increased venous pressure and polycythæmia, these in turn being due to the chronic chest condition (emphysema and chronic bronchitis). The possibility of pulmonary arteriosclerosis had been mentioned by the radiologist. Intracranial tumour and hypertensive retinopathy appeared to be ruled out.

He had seen a similar case with secondary optic atrophy before the war at the London Hospital, when the possibility of a cerebral abscess secondary to the chest condition had been mooted.

Cases of polycythæmia had been recorded in the literature with increased cerebrospinal fluid pressure and papillœdema, the latter indistinguishable from that which occurs in intracranial tumour. The matter was complicated by the fact that subdural hæmatoma might occur in polycythæmia.

Sir Charles Symonds said that he had seen a fundus exactly like this in primary polycythæmia, which he thought supported the view that that was the cause. He had observed very severe headaches as a symptom of obstruction of the superior vena cava but not papillœdema.

Poliomyelitis Limited to both Trigeminal Motor Nuclei.—DENIS WILLIAMS, M.D.

A boy aged 6½ years was brought to the National Hospital in January 1947 because he had been unable to chew since an acute febrile illness eighteen months previously.

In July 1945 he had an acute fever with meningism and semi-coma from which he recovered in a few days. His mother then noticed that he was not chewing normally. In September 1945 (six weeks after onset of weakness) he went to the Hospital for Sick Children where it was found that he had indistinct speech and complete inability to chew. The only abnormality found in the central nervous system was marked weakness of the pterygoid and masseter muscles on both sides. All tendon-jerks normal; no weakness of any other muscles. Complete R.D. in both masseters. He was observed each month until March 1946 but no change was found.

On examination in the National Hospital, his nervous system was normal throughout

Dr. Carmichael replied that, as to the first question, the reflexes were exceedingly brisk. As to cortical atrophy, his radiological colleagues told him that there was no sound evidence of this, though there might be some atrophy in the frontal region. Davison and Keschner (*Arch. Neurol.* 1940, 43, 524) had described a somewhat similar case in which they had found "inclusion" bodies in the nerve cells. There was no family history in this case of similar disturbance.

Dr. J. G. Greenfield stated that this question of inclusion bodies dated back for a long time before the paper in the *Archives of Neurology* to the observation of Lafora and Westphal, but he did not know whether the cases they described were clinically similar to the present case or not.

The President said that mental deterioration was rather characteristic of myoclonus, i.e. epilepsy, and asked whether this was considered a normal case in that respect.

Dr. Carmichael replied that this man was at one time euphoric, but was now depressed. When admitted, he was put on phenobarbitone and similar preparations; heavy doses were given without improvement. He was then taken off these drugs and given benzedrine, on which he showed some improvement. He was, however, now going downhill.

Spontaneous Carotid-cavernous Aneurysm.—S. P. MEADOWS, M.D.

Miss J. D., aged 56. October 1944: Sudden onset of throbbing noise in head, especially right ear, which persisted.

January 1945: Right upper lid became swollen, followed by increasing exophthalmos and redness of right eye.

April 1945: Pain right side of forehead and upper jaw, associated with a cold feeling over the same area. Epistaxis lasting an hour.

No diplopia or loss of vision. General health good.

Past illness.—1935: She was knocked down in the road, and was unconscious three hours and in hospital two weeks.

On examination (May 1945).—R. proptosis (6·5 mm.). No definite pulsation seen. Chemosis and engorgement of vessels of R. conjunctiva. Slight weakness of R. external rectus muscle. Retinal veins engorged in R. optic fundus.

Loud systolic bruit heard over right side of head and face, which almost ceases on compression of right common carotid artery. B.P. 220/125.

After about two weeks of daily digital compression of the right common carotid artery in the neck for periods up to thirty minutes, the right common carotid artery was ligated on June 3, 1945. This was followed by increase in the chemosis and exophthalmos, and the development of a third cranial nerve paresis (dilated, sluggishly reacting pupil, weakness of elevation and adduction of the right eye, and partial ptosis and sixth cranial nerve palsy). About ten days after the ligature, retinal hæmorrhages were noted scattered over the right retina, with papillœdema. The cephalic bruit persisted after ligature, but was fainter and more localized. The exophthalmos, chemosis, ocular palsy, and retinal hæmorrhages slowly subsided.

Present condition.—V.A.: R. 6/9 partly with glasses. Right optic fundus: No hæmorrhages. Disc slightly blurred. Ocular movements full. No ptosis. R. pupil slightly larger than L. and reacts well. Slight R. exophthalmos (about 3 mm.). Congested conjunctival veins. B.P. 235/115. Systolic bruit heard over R. eye, fainter than before ligature.

Dr. Meadows said that some of these cases healed spontaneously. One such case was an elderly woman in whom the bruit disappeared and the exophthalmos improved after repeated digital pressure on the common carotid artery. Another case was a dramatic one, that of a man who had bilateral exophthalmos and chemosis and one could not be sure on which side the aneurysm was, except by the lateralization of the bruit. On first inspection it resembled the exophthalmos of Graves's disease. An interesting point was why some of these cases had bilateral exophthalmos with a unilateral aneurysm. He thought it was due to the circular sinus which connected the two cavernous sinuses, and which varied in its patency in different individuals.

The President said that recently he had a similar case in a woman aged 75 who showed bilateral sixth nerve palsy. The bruit was heard well on both sides of the head. There was no exophthalmos and only a mild degree of chemosis on the right side. Presumably the bilateral signs were due to arterial blood reaching the opposite cavernous sinus via the circular sinus. On account of her age carotid ligature was considered inadvisable. He hoped that Dr. Meadows would publish the cases he was collecting since the correct treatment for this somewhat rare condition was still in douht.

Dr. Purdon Martin had seen two cases in which there had been a thrombosis of the cavernous sinus after rupture had occurred. One of them came to post-mortem later and it was possible to confirm the diagnosis. The other patient lost all ocular movements and became blind; about a week later he recovered and was said to have left hospital quite well. Recovery was certainly possible.

Dr. Meadows, in reply to Dr. Purdon Martin, who asked whether any good was done to this patient by tying her carotid, said that before operation the proptosis was increasing considerably, and she was complaining bitterly of the bruit. Now she was very much better, the exophthalmos had almost disappeared, and the faint bruit did not trouble her.

Papillœdema associated with Chronic Bronchitis, Emphysema and Polycythæmia.—S. P. Meadows, M.D.

D. G. R., male, aged 42. Chief complaint is that of insomnia for past few years, due to bronchitis. Recurrent bronchitis with asthmatic attacks for over twenty years, worse during the winter. Dyspnœa on exertion past few years. Morning headaches when he sleeps badly.

On examination.—Obese, plethoric, cyanosed man. Moderate dyspnœa on exertion. No finger clubbing. Bilateral papillœdema with hæmorrhages scattered about the retinæ. V.A. 6/9. Visual fields full. No other abnormal signs in C.N.S. Lumbar puncture: C.S.F. pressure 240 mm. C.S.F. normal. Chest: Poor expansion, poor air entry with expiratory wheezings. Heart clinically normal. B.P. 140/80. No congestive failure. E.C.G.: Right ventricular preponderance. He had a short attack of auricular fibrillation while in hospital in December 1946.

Ventriculogram: Normal ventricular system. X-rays: Skull normal. Chest: Well-marked emphysema with very poor expansion of lungs and practically no diaphragmatic movements. Slight cardiac enlargement, both right and left ventricles. Main pulmonary artery and its branches are dense. The appearances may be due to pulmonary arteriosclerosis. Vital capacity: 1,562 c.c. (about 1/3 normal). Renal function tests normal.

Blood-count: Shows polycythæmia. R.B.C. 8·22 million and 6·82 million on different occasions, with 134% and 116% hæmoglobin.

Dr. Meadows suggested that the papillœdema in this case was secondary to the chronic increased venous pressure and polycythæmia, these in turn being due to the chronic chest condition (emphysema and chronic bronchitis). The possibility of pulmonary arteriosclerosis had been mentioned by the radiologist. Intracranial tumour and hypertensive retinopathy appeared to be ruled out.

He had seen a similar case with secondary optic atrophy before the war at the London Hospital, when the possibility of a cerebral abscess secondary to the chest condition had been mooted.

Cases of polycythæmia had been recorded in the literature with increased cerebrospinal fluid pressure and papillœdema, the latter indistinguishable from that which occurs in intracranial tumour. The matter was complicated by the fact that subdural hæmatoma might occur in polycythæmia.

Sir Charles Symonds said that he had seen a fundus exactly like this in primary polycythæmia, which he thought supported the view that that was the cause. He had observed very severe headaches as a symptom of obstruction of the superior vena cava but not papillœdema.

Poliomyelitis Limited to both Trigeminal Motor Nuclei.—Denis Williams, M.D.

A boy aged 6½ years was brought to the National Hospital in January 1947 because he had been unable to chew since an acute febrile illness eighteen months previously.

In July 1945 he had an acute fever with meningism and semi-coma from which he recovered in a few days. His mother then noticed that he was not chewing normally. In September 1945 (six weeks after onset of weakness) he went to the Hospital for Sick Children where it was found that he had indistinct speech and complete inability to chew. The only abnormality found in the central nervous system was marked weakness of the pterygoid and masseter muscles on both sides. All tendon-jerks normal; no weakness of any other muscles. Complete R.D. in both masseters. He was observed each month until March 1946 but no change was found.

On examination in the National Hospital, his nervous system was normal throughout except that there was no demonstrable contraction of the temporal muscles, the masseters or the external pterygoids. There was jaw drop with no power in opposition of the jaws. The muscles supplied by the fifth nerve which are responsible for opening the jaw were in sharp distinction to those responsible for closing it in that power was fairly well preserved. There was a suggestion of slight weakness in the perioral muscles; all other muscles powerful; tendon-jerks brisk and equal.

The interest of the case is that the poliomyelitis virus had picked out almost exclusively that part of the motor nucleus of the fifth nerve on both sides which is responsible for closing the mouth.

The President said that this was a rare case. In his experience of acute poliomyelitis overseas during the war he had only come across four cases which showed this sequel. Three of the four cases had shown other brain-stem signs initially. In one case he had noted relative sparing of the pterygoids as in the present case. In this selective action of the virus he was reminded of a case of a Medical Officer who showed, as a sequel of the disease, bilateral paresis of the sternomastoids with sparing of the trapezii.

Dr. A. S. Hollins said that he saw a similar case in the Mediterranean in 1943 in a young medical officer from Sicily. He had had an acute febrile illness with intense headache, which was followed by weakness of the muscles of mastication. When seen in North Africa he had an almost complete palsy of the masseters, temporals and pterygoids on both sides. He had made almost a complete recovery when he was allowed to leave hospital for a convalescent wing.

Wilson's Disease.—Denis Brinton, D.M.

Joan S., aged 21. Single.

June 1940: Jaundice with fever, hæmolysis and reticulocytosis; discharged from hospital after three months with diagnosis of "Subacute hepatitis with recurrent bouts of pyrexia." Thereafter amenorrhœa till 1946.

1944: Won exhibition Cambridge. Shortly after, jaw kept dropping open and saliva dribbled.

1945: Walking difficult, handwriting deteriorating, involuntary movements arms and head, speech indistinct; chorea diagnosed.

1946: Steady deterioration, though intensity of each symptom widely variable; difficulty in mastication and deglutition; Kayser-Fleischer ring found.

1947: Speechless; painful spasms of arms; virtually bedridden.

Dr. Denis Brinton added that the case formed quite a good example of Wilson's disease. The patient's brother, who was about four years younger than she, had a very similar story of jaundice with recurrent fever; this happened about two years after the patient's first symptoms. Each of these siblings had had obvious jaundice of the skin and sclera, pale fæces, and a marked hæmolytic anæmia. The girl had had a blood-count in 1940 as low as 1,670,000 red cells and 35% hæmoglobin, with reticulocytes at 11%. In the brother's case the reticulocytes were 6%, and his anæmia was not so severe—3,000,000 red cells, with a 70% hæmoglobin.

He showed pictures of the Kayser-Fleischer ring in both the patient and her brother. The patient was now incapable of movement except on rare occasions. She had virtually lost her power of speech, and she was troubled by exceedingly painful spasms of the arms. If tension were placed on the flexed fingers a curious rhythmic contraction occurred. At an earlier stage the opinion had been entertained that the aphonia was of an hysterical kind, but that was obviously not the case. The tremor had a regular rhythm, suggesting extrapyramidal trouble.

A recent test at St. Mary's had suggested that her liver function was within normal limits. In the case of her brother both liver and spleen were palpable. This patient's liver was not palpable. The brother showed some slurring of speech and some facial immobility. Some investigations had been recently carried out on the blood copper, because Glazebrook (*Edin. med. J.*, 1945, 52, 83) had suggested that this might be important; in the girl's case, however, the blood copper was within normal limits. In reply to a question Dr. Brinton said that at the time of the jaundice no tests had been done for any form of antibody.

Dr. Purdon Martin said that this patient had a peculiar tremor which seemed to be due to clonic contraction of the flexors. He was interested also in the variability of her rigidity and her ability to speak first thing in the morning. There was evidently in the early morning a reduction in rigidity. Some patients with extrapyramidal rigidity were almost free from rigidity on waking in the morning and were able to dress themselves.

Section of Obstetrics and Gynæcology

President—JAMES WYATT, F.R.C.S., F.R.C.O.G.

[*March* 21, 1947]

DISCUSSION ON ANÆSTHESIA FOR CÆSAREAN SECTION

Mr. Rufus C. Thomas: The essential criteria for any anæsthetic for Cæsarean section must be, primarily, safety for the mother and child, and, subject to these, ease of operating for the surgeon.

I propose as my contribution to this discussion to give details of my experience of spinal anæsthesia induced with heavy nupercaine, under which almost all my Cæsarean sections have been done for the past nine years. At the same time, I do not wish to convey the impression that I think spinal anæsthesia is suitable for any and every woman. Briefly, the arguments against spinal anæsthesia in the case of pregnant women are these:—

(1) Pregnant women at or near term are supposed to be highly susceptible to the effects of the cocaine products. If this is so, the answer is that nupercaine is a quinoline compound, and is not related to the cocaine group.

(2) That collapse and sudden death are liable to occur from a sudden drop in blood-pressure due to paralysis of the vaso-constrictors and dilatation of the splanchnic pool. That might be so, if proper precautions are not taken, but this danger can be avoided, by giving ephedrine, ¾ grain before the spinal injection, by careful positioning of the patient to ensure that the solution does not rise above D.8 (this gives anæsthesia nearly up to the ensiform cartilage, which is ample for a Cæsarean section), by having the blood-pressure recorded at five-minute intervals throughout the operation, by the injection of methedrine, 15 mg. into the uterine muscle if the systolic pressure drops below 90 mm.Hg (methedrine acts very quickly by this route, and produces by peripheral vaso-constriction a sustained rise of blood-pressure up to or above the normal), and, finally, by the elementary precaution of not using spinal anæsthesia in unsuitable cases. For instance, cardiac disease with decompensation is, I need hardly say, an absolute contra-indication. It is dangerous to use spinal anæsthesia in cases of severe anæmia and low blood-pressure, unless and until the patient's condition can be restored by blood transfusion and other means. Severe anæmia and low blood-pressure may be met with in women who have had hæmorrhage from placenta prævia. But such cases can, by blood transfusion, be rendered fit for spinal anæsthesia, as I hope to show by my figures later.

(3) That a number of cases of meningitis, some of them fatal, have followed the use of spinal injections. One possible explanation was that the technique of manufacture might be faulty. I have watched the whole process in the laboratories. The precautions are so rigid that such a possibility is inconceivable. The theory of aseptic or chemical meningitis has never been proved, and Frankis Evans says that it must be treated with extreme caution. There remains the explanation of faulty technique in the preparation of the syringes, needles, hands of the anæsthetist, the ampoules, and the skin of the patient in giving the injection. The answer is that the procedure should be as rigidly aseptic as the Cæsarean section itself.

(4) The last objection is the incidence of post-operative headache. This does occur. In my view, it is due to leakage of cerebrospinal fluid through the puncture in the theca. If I am right, it can be reduced by using the finest needle, keeping the patient flat for twenty-four hours, and raising her very gradually to the semi-Fowler position.

The advantages of spinal anæsthesia under heavy nupercaine are:—

(1) If the precautions already outlined are taken, it is safe for the mother and is easy to administer. The only difficult cases are those with spinal deformities. The patient feels nothing after the initial prick of the needle when anæsthetizing the track. For this, 1 : 1,000 nupercaine with adrenaline, in 5 c.c. ampoules, is used.

(2) The amount of movement necessary is very small. She lies on her side when the injection is given, then turns on her back, or can be turned by the theatre staff without any effort of her own, an important point in cases of placenta prævia. The head and shoulders are raised, and the table tilted in the Trendelenburg to about 7 to 10 degrees. After five minutes the table is straightened and the operation can be proceeded with.

(3) The patient is, of course, conscious, hears her baby cry at birth, can be told its sex, and can even see it for herself. To many women, this is a great satisfaction. She can have drinks while being operated upon and after returning to the ward, and can see her husband immediately.

(4) The anæsthetic has no effect whatever on the baby. I have known many infants cry lustily before they were completely removed from the uterus. The advantage of this, especially in cases of fœtal distress, is obvious.

(5) The surgeon has the maximum of operative comfort. The muscles are completely relaxed, the abdomen is quiet, and abdominal packs can be placed in position with the greatest ease. Access to the lower segment is greatly facilitated. Uterine tone is excellent, there is very little bleeding, and, in fact, many operations are practically bloodless. The placenta often delivers itself. Closure of the uterine and abdominal incisions is easy.

(6) The post-operative period, apart from possible headache, is very comfortable. Vomiting and distension are rare, and chest complications practically non-existent.

I should like to give a few further details of the technique I employ.

Premedication.—Ephedrine, ¾ grain and atropine, 1/100 grain are given forty minutes before operation. Atropine is given in case the spinal has to be supplemented, but apart from an occasional nervous woman, this is rarely necessary. No sedative is given.

Sterilization of needles, syringes, and ampoules.—Needles and syringes are boiled in sterile distilled water, and stored ready for use in industrial spirit. The ampoules have, at present, paper labels. These are a source of danger. They are washed off with hot water and soap, the ampoules then rinsed in cold water, and stored in industrial spirit. This eliminates the danger of infection from the gum. I am informed that the etching of the description and dosage on the ampoules will be resumed shortly.

The skin of the patient's back is prepared in the ward by washing with ether soap, painting with spirit, followed by 1% flavine, and covered with a sterile towel. Before the spinal injection, it is again painted with spirit. The hands of the anæsthetist are, of course, prepared as for any surgical operation.

By a scrupulous adherence to this technique, there should be no risk of septic meningitis. We have now given well over 2,000 spinal anæsthetics for obstetric and gynæcological operations, and have not seen a case of meningitis.

In passing the spinal needle, I believe it is important, having carefully located the exact site, to push the needle steadily but slowly on in one continuous movement until the point is felt to pierce the theca. This moment can actually be felt if the operation is deliberate enough. Haphazard poking about must be avoided.

The amount of heavy nupercaine injected is 2 c.c. in most cases, though I have used 1·75 c.c. occasionally in very short women. The space for injection is between the third and fourth lumbar spines. If blood-stained cerebrospinal fluid is found, the next space up is used.

Up to date we have performed 346 Cæsarean sections under heavy nupercaine anæsthesia. Of these, 314 were lower segment operations, and 32 were classical. There has not been a maternal death either under or due to the anæsthetic.

The number of infants delivered, including four sets of twins, was 350. Of these, 2 were stillborn, and 10 died. The infant salvage rate is therefore 96·6%.

The chief indication for operation was disproportion, a large number of women having had a test of labour first. But we have used spinal anæsthesia now in practically all the recognized indications for Cæsarean section, including a number of cases complicated by ovarian cysts, for the removal of which the length of anæsthesia is ample. It is also worth noting that 58 sections have been done for cases of placenta prævia, showing that these patients can, by blood transfusion and other means, be rendered fit for spinal anæsthesia.

Finally, we have done Cæsarean sections under spinal analgesia twice for 41 patients, and three times for 5 patients. This suggests that the women themselves do not object to this form of anæsthesia.

Mr. J. H. Peel: My contribution is to report on a small series of cases in which the operation has been carried out under caudal anæsthesia. I do this not so much from the belief that caudal anæsthesia is necessarily the perfect and universally applicable anæsthetic, as from the conviction that this method is a very valuable addition to the anæsthetist's armamentarium in the preparation of patients for Cæsarean section. I think that this applies more particularly to the systematic and unhurried approach to the lower segment, than to the more rapid, less artistic and potentially more dangerous classical operation.

The dangers of ether, chloroform, pentothal and other anæsthetic agents in causing fœtal narcosis, and of nitrous oxide in producing fœtal anoxia are too well recognized to require emphasis. There seems to be a gradually growing conviction, both in America and in this country, against the use of general anæsthesia for Cæsarean section. Lull states (Control of Pain in Childbirth, London) "Our results at the Philadelphia Lying-in Hospital in the use of the anatomic approach in these cases over a period of several years, and totalling approximately 350 cases, have been so satisfactory that at the present time we resort to general inhalation anæsthetics only in a minority of cases, and we are of opinion that as the technique of giving fractional spinal and continuous caudal is developed and mastered by more men interested in this phase of medicine fewer women will be subjected to inhalation anæsthesia at the time of Cæsarian section." He goes on to state that he has spent three years in an endeavour to evaluate the difference between continuous caudal and fractional spinal in these operations and at present has not decided whether there is any real difference. I am not an anæsthetist and it is not for me to dwell on this point. I maintain an open mind and am quite prepared to admit the advantages of spinal. Both the American figures and those quoted by Mr. Thomas are excellent and very convincing. It is difficult, however, to dissociate one's mind from personal experience of disasters encountered where spinal anæsthesia has been used, and caudal anæsthesia completely obviates the risks of meningitis, nerve palsies and post-spinal headaches, as well as the occasional more disastrous sequel of immediate post-operative collapse and death.

I am indebted to Dr. A. H. Galley primarily for the opportunity of employing caudal anæsthesia for Cæsarean section. Briefly, the method consists of the injection of 50 to 100 c.c. of 1½% metycaine into the sacral canal via the sacral hiatus. A special malleable needle devised by Hingson and Edwards is used. Precautions against tapping the subarachnoid space placed abnormally low are taken, and if care is taken against too rapid injection of the fluid and the injection of quantities larger than are required to produce anæsthesia to the level of the umbilicus is avoided, completely satisfactory anæsthesia is induced without risk to the patients—mother or child. The technique sounds simple enough, but without question herein lies the one and chief difficulty of the method. Lull states that 10% of sacra show anatomical abnormalities which may preclude the successful employment of the method. In my experience there are probably another 10% to 15% in whom there is so much adipose covering to the sacrum that identification of the hiatus is difficult or impossible. Therefore, it can only be by persistent trial and experience that anyone will attain a degree of skill sufficient to employ this method with the certainty of achieving good results. Further I would say that even with complete familiarity with the technique it must take from twenty to forty minutes from the start of the injection to the moment when the patient is ready for the surgeon. But even admitting the difficulties in technique and practical drawbacks, the successful result, when obtained, is so perfect —from my point of view as the surgeon and from my patients'—that I am convinced the method merits a far more extensive trial than it has yet been given in this country.

I will give you a brief résumé of cases we have done at King's College Hospital. There are 51 cases in all. In addition there have been a number of cases in which failure has occurred, due in every instance to technical difficulties in the insertion of the needle. In the 51 cases the operation was performed successfully without any additional anæsthetic agent. Table I shows the indications for operation and illustrates a fairly wide applicability. The high incidence of diabetes in this list is due in part to our very dense population of diabetics at King's, but also it is because this method is particularly valuable for these difficult cases.

TABLE I.—INDICATION FOR OPERATION (51 CASES)

Diabetes	15	Breech with extended legs and contracted pelvis	2
Contracted pelvis	10	Chronic nephritis	1
Cardiac disease	7	Hyperemesis	1
Severe pre-eclamptic toxæmia	6	Prolapsed cord	1
Age with other factors	3	Pulmonary tuberculosis	1
Obstruction due to fibroids	2	Following repair of recto-vaginal fistula	1
Obstruction due to ovarian cysts	1		

There has been no maternal mortality, and no higher incidence of morbidity than is experienced in any series of Cæsarean sections. There were no stillbirths. Three neonatal deaths occurred, due to prematurity in one case (32 weeks), and to the diabetic condition of the mother in two. The majority of these operations were "set" Cæsareans, but in a few the patient was in labour at the time of the operation.

In conclusion I will indicate the more important and salient points about the method:—

(1) The operation can be performed without any hurry to extract the child for fear of narcosis or anoxia.

(2) Hæmorrhage from the uterine incision and from the placental site is minimal. It is perhaps the most striking feature of the operation performed with this method of anæsthesia.

(3) The baby cries immediately. There is no narcosis, no anoxia. This is particularly important in cases where the baby is premature. Atelectasis, pneumonia following inhalation of liquor, are reduced to a minimum.

(4) The Trendelenburg position can safely be used. This is often a great help in performing the lower segment operation. This is a small but important advantage over spinal using heavy nupercaine.

(5) A transverse incision through the abdominal skin and rectus sheath, which heals so well subsequently, can with greater safety be employed than when using general anæsthesia, because bleeding is less and time does not matter.

(6) With regard to premedication we have tried every conceivable premedication compatible with reasonable safety to the child. I have come to the conclusion that patients are far more co-operative and less worried if they have no premedication at all than if they have small doses of drugs which render them so often excitable. Larger doses are obviously more dangerous to the child.

(7) Success can only follow careful selection of cases, especially from the psychological angle.

(8) Apart from local abnormalities and difficulties in locating the sacral hiatus, the two most important contra-indications are recent hæmorrhage and low blood-pressure.

(9) Lull advocates giving ephedrine 25 to 50 mg. routinely. We have not done this and in only few patients have we experienced any appreciable fall in blood-pressure.

(10) Oxytocic drugs are unnecessary—in fact undesirable, as the uterus may contract so vigorously that the patient experiences severe uterine cramp after the analgesic effect of the caudal wears off.

(11) The patient should be given morphia ¼ grain, after the baby is born and in any case before she leaves the theatre.

(12) The immediate post-operative period is infinitely smoother than that following the use of general anæsthesia, and chest complications in particular are minimal.

(13) By far the most important drawback to the method is that it requires an expert, experienced in this particular technique, to administer the injection. The technique is difficult, but from the point of view of the surgeon who has to do the operation and look after the patient subsequently I would urge that this method be given a more extensive trial, especially by those who are of opinion that spinal anæsthesia is dangerous for women during pregnancy.

Mr. C. McIntosh Marshall (*Liverpool*): Some eight years ago when I wrote on this subject I had had a fairly extensive experience of the three main anæsthetic methods: inhalation, spinal and local. Though that experience has greatly increased there is nothing I should really like to retract while there is much I would heavily underline. But that chapter has also placed me in certain difficulties; it has brought me many personal communications and visitors. I have sometimes felt how much better it might have been had I been able to set down such confidential and "off the record" revelations, and when I think of the matter which is under discussion to-night I am quite unable to put out of my mind all those things I have heard out of court.

Of sacral anæsthesia I have had no experience. In one obstetric unit for which I am responsible I allow my anæsthetist to give *pentothal-curare-cyclopropane*. I am thus enabled to claim that I have a small but useful experience of the anæsthetic combination which some are already maintaining is the ideal one for this operation. These are three very powerful drugs and they are now available for all, and there I leave them, remembering what Beecher wrote in 1938: "Whenever an anæsthetic has enough good qualities to get it past an early trial period it seems to take about ten years to evaluate its bad effects."

To my mind there are several reasons why *inhalation anæsthesia* is unsatisfactory and even dangerous. I would place first those accidents during induction which seem so prone to occur in obstetrical anæsthesia. In the interests of the child pre-operative sedatives must be given with caution, the plane of anæsthesia is intentionally rather light than deep, the risk of vomiting and the aspiration of stomach contents into the bronchial tree is a very real one. I know of three deaths from this cause while I have seen a number of non-fatal cases of severe aspiration pneumonia, the most recent occurring after a forceps delivery only a few weeks ago. In the excellent papers by Mendelson (1946) and by Hartzell and Mininger (1946) this particular risk has at last received the publicity which I feel it surely merits. Further, most inhalation anæsthetics induce some degree of anoxia, of little importance as a rule. But if as a result of laryngeal spasm or vomiting the mother becomes temporarily cyanosed, the anoxic state is quickly reflected in the infant and a stillbirth or a neonatal death from atelectasis can result. Even in cases in which none of these mishaps arises many babies come under the influence of the anæsthetic and some resuscitation is required, and in the very occasional one this is not successful. There are, too, the effects of inhalation anæsthesia on uterine tone, none of them actually stimulating while some are certainly the very reverse. However, by timely and adequate administration of oxytocic drugs these disadvantages can usually be counteracted. Admittedly, in the perfectly sound woman operated on before the onset of labour, the dangers we have mentioned, while real, are not likely to occur often with the expert anæsthetist. It is, however, a strange and perverse fact that when a fœtal tragedy does occur it always seems to fall upon an elderly primigravida after some ten or fifteen years of infertility.

When, on the other hand, labour has been prolonged, when poor uterine action has been a prominent feature, when large amounts of sedatives have been used, when the membranes have been ruptured many hours and extreme moulding is present or there are frank signs of fœtal distress—then one or other of these dangers is much enhanced and general anæsthesia is, in my opinion, absolutely contra-indicated. It is among such patients that most of the immediate mortality of Cæsarean section falls. The prolonged emptying time of the stomach should be borne in mind ; blood loss is apt to be increased, temporary collapse and even death from shock are not uncommon. The fœtal risk requires no emphasis—it is always very great and is certainly not improved by inhalation anæsthetics. The only justifiable choice lies between spinal and local anæsthesia. Spinal is almost ideal for reasons which I need not recapitulate here. It *is* ideal if we can believe that with newer drugs and a perfected technique sudden collapse and death need never occur. Individual obstetricians can produce large series with none of these strange and almost unexplained fatalities. Only one has occurred in my own hospital. I still use the method and have not suffered a death but even with a minimal dose I occasionally meet a degree of collapse which is disturbing and deaths still appear in the literature—the latest to my knowledge being the one reported last October by A. E. Brown (1946). Unfortunately by no means all the deaths in this country due to spinal anæsthesia in Cæsarean section find their way into the literature. I use spinal in cases in which I can foresee special technical difficulties, in very large and obese women who support the method extremely well, and in the performance of an occasional extraperitoneal section. I have never seen spinal anæsthesia have the slightest adverse effect on the fœtus. Accidents can probably be avoided by the use of the minimal dose. It is for this reason, I believe, that its dangers do not manifest themselves when used for vaginal deliveries. With Anderson (1946) I fully agree that its use should be greatly extended among all those patients requiring difficult instrumental delivery.

I am, however, still unable to disbelieve the evidence of my eyes. *Local* is pre-eminently the anæsthetic of choice for the intraperitoneal lower segment operation. Few will deny its great value in patients who are poor surgical risks, in those who have a toxæmia, are suffering from pulmonary or cardiac disease or have a high grade anæmia. And yet—and here is a paradox I would rather not attempt to explain—a patient who is fit and sound in every way is by most of us denied the safest of all anæsthetics and must accept a procedure which will place her in some degree of jeopardy, however slight this may be. I could comprehend this attitude if from time to time there appeared accounts in the literature of tragedies due to the use of local infiltration methods in the operation. It is just the reverse; on such things the literature is absolutely silent. Among the hundreds of contributions to the subject of to-night's discussion one still remains unwritten: "The Dangers of Local Anæsthesia in Cæsarean Section." I do not believe that it will ever appear for those who use the method will have no cause and those who have not employed local will lack the courage to publish such an article. But I do not wish to give a false idea of my own practice. Over the years I quite frequently use an inhalation anæsthetic. "Video meliora, proboque; deteriora sequor." Were this discussion devoted to the reasons why local anæsthesia is not more widely used I would be only too glad to express myself more fully upon these lines by Ovid. It is unlikely that many obstetricians will ever extend this form of anæsthesia to the majority of their patients. Yet there is the clearest evidence that up and down the country interest in the method is increasing. I would make a serious plea that at least it should be considered in all patients mentioned above, in those with diabetes or other medical disorders and particularly when it is important to give the premature child every chance of survival. It is the anæsthetic which promises the normal and therefore the best oxygen supply in the mother's blood so long as the baby is dependent on the placental circulation.

For many years now, as a result of certain fœtal misfortunes, I have given no pre-operative sedative. Some received morphia ¼ grain at the beginning of infiltration, others receive nothing at all. On the other hand in order to ameliorate some of the rigours of local and to speed closure of uterus and abdominal incision I have someone give a little pentothal just before I incise the uterus. So far I have seen no harm result to mother or child and the patient is usually awake when the dressing is being applied. The specific advantages of local have been set out so well and so often by De Lee, Greenhill and others that I shall not repeat them here. There is only one word of warning and it concerns a technical point. When dealing with an uncorrected transverse presentation, never open the lower segment under local alone. The back, or the shoulder and an arm fall into the wound, and extraction may be almost impossible.

We are probably all agreed that in the present-day tendency to abolish all or most of the pain of childbirth there arise certain dangers for both mother and child. After all, and this is too often forgotten, the expectant mother is on the whole a most reasonable person. With simple and honest explanations her confidence can be won and she will no longer insist that safe delivery, whether vaginal or abdominal, should be entirely free from pain or discomfort.

REFERENCES

ANDERSON, A. R. (1946) *J. Obstet. & Gynec.*, **53**, 347.
BROWN, A. E. (1946) *Med. J. Aust.*, **2**, 488.
HARTZELL, C. H., and MININGER, E. P. (1946) *Surg. Gynec. Obstet.*, **82**, 427.
MENDELSON, C. L. (1946) *Amer. J. Obstet. Gynec.*, **52**, 191.

Dr. Katherine Lloyd-Williams: I propose to refer to the records of 305 cases done over a period of several years in the Obstetrical Department of the Royal Free Hospital. They fall into a pre-war series of 224 between 1931–39, and a post-war series of 81. During the war most midwifery was transferred from London, the Obstetrical Unit of the Royal Free was scattered, and though I was able to give the anæsthetics for Cæsarean section on many occasions at some of the outlying hospitals, I have no such full and continuous records of cases done in the war period.

TABLE I.—1931-1939. ANÆSTHETICS USED IN 224 CASES OF CÆSAREAN SECTION

Spinals:		
Stovaine 10%	10	85
Nupercaine 1 : 2,000	75	
Chloroform→ether		22
Ethyl cloride→ether		71
Gas and oxygen + some other anæsthetic (ether, vinyl ether, trilene, chloroform, evipan)		43
Cyclopropane		3

There were no maternal deaths.

TABLE II.—1945-46. 81 CASES (50 CLASSICAL C.S., 31 LOWER SEGMENT)

Anæsthetics used:	
Intravenous pentothal, gas and oxygen + trilene or ether	78
Caudal block	1
Local anæsthetics	2

There were no maternal deaths.

Infant mortality:
1945: No stillbirths.
2 died within twenty-four hours (1 atelectasis, 1 due to cerebral congestion from tight cord round neck. C.S. for fœtal distress).
1946: 1 stillbirth. Mother diabetic. Child probably dead before operation.
3 died within twenty-four hours—all atelectasis (1 premature).

I will describe briefly the methods I used from 1928 onwards and what caused me to modify these methods.

In common with many of my generation I had no experience, when I qualified, of chloroform anæsthesia beyond the occasional few drops on a mask in the maternity wards for delivery. I was little better off after several months of being a resident anæsthetist and, like many others, I finally taught myself in fear and trembling, often, I see when I look back, on highly unsuitable cases. When first confronted with anæsthetics for Cæsarean section, I determinedly chose the anæsthetic which I felt I could give, i.e. ethyl chloride → open ether. No great depth of anæsthesia is required for the classical Cæsarean section which was the routine method in vogue, and on the whole this appeared to serve very well as far as the operation was concerned. I rapidly found, however, that the resuscitation of the baby frequently fell to my lot. It often took quite a long time to get respiration well established. I therefore began to use chloroform until the baby was delivered and then changed over to ether. Results were not always consistent, but I nevertheless convinced myself that the babies were not so slow in starting to breathe as when ether was used throughout.

Gas and oxygen came into common use and I pursued much the same course. If I could, I gave gas and oxygen until the baby was born but rather than push the anæsthetic (and even at this time to my mind nothing was more disastrous than "pushing" this anæsthetic, so cutting down the oxygen supply), I passed the gases over chloroform and after delivery deepened the anæsthesia by giving gas and oxygen and ether.

Gas and oxygen were often sufficient alone but in heavy plethoric cases it is obviously insufficient and the addition of ether was, more often than not, necessary for the closing of the peritoneum after the pelvis had been swabbed out.

I would at this point say that though in the large majority of cases both the operation and the anæsthetic for Cæsarean section are comparatively easy procedures, in my opinion there is no operation which is so dependent on complete confidence and co-operation between surgeon and anæsthetist. Almost all the obstetricians with whom I have worked prefer extremely light anæsthesia until delivery, and the minimum of abdominal investigation is done prior to this. If a surgeon requires deep anæsthesia throughout, the anæsthetist must adjust his technique accordingly.

I next tried spinal analgesia, first using 10% stovaine and later nupercaine. From the surgeon's point of view these results were very satisfactory. At this time I had not heard of rachi-sensitive subjects (as pregnant women are said to be) but nevertheless, being of a cautious nature, I obtained a 1 : 2,000 solution of nupercaine (instead of the usual 1 : 1,500) for the maternity wards, 11 to 13 c.c. being a usual dosage. Spinal anæsthesia for some time became the routine method for Cæsarean sections in the department preceded by a small dose of omnopon and scopolamine, unless the fœtal heart was not satisfactory or the baby was premature. This was followed post-operatively by paraldehyde 5 to 6 ℥ P.R. We thought there was less post-operative distension and discomfort by avoiding morphia and we also discouraged the intake of excess fluid and persuaded the patients to take solids as early as possible. This was easier where a spinal alone was used, as was frequently the case. If the patient was highly nervous she was given gas and oxygen, but the diaphragmatic breathing induced by this was not popular. Spinal anæsthesia has had a bad name for Cæsarean section since Dr. Fairfield's report in 1937 (*Proc. R. Soc. Med.*, 31, 237) in which she says that in a series of 781 Cæsarean sections there were 3, possibly 4, deaths due to spinal anæsthesia in the L.C.C. hospitals.

There is no record of the number of Cæsarean sections in which spinal anæsthetics were used but in this series of 781 cases no other form of anæsthesia caused death. I am glad to record that in our series of cases no deaths occurred, nor, once we had begun the use of nupercaine, had we cause for anxiety over patients. Complications such as backache or headache were common with stovaine, though I think as these were the early cases they were most probably due to faulty technique.

When the lower segment operation became common, spinals became less popular—or perhaps it was partly Dr. Fairfield's report. This is usually a more prolonged procedure and involves more manipulation which puts a considerable strain on the patient. We also thought the baby more difficult to extract because of the contraction of the uterus. We tended, therefore, at this time, to return to general inhalation methods with its disadvantages, and this accounts for the rather large number of ethyl chloride→ether in the table. Though we kept records throughout of the time taken to establish the baby's respiration I feel unable to make any definite statement from the records that one anæsthetic caused more delay than another.

The war years were a transition period and a time of experiment on the comparatively few cases we had. Cyclopropane was an obvious choice from the point of view of the baby, but surgeons thought it caused excessive bleeding. Gas and oxygen with trilene, chloroform, vinyl ether, ethyl ether were all in use at one time or another, most usually preceded by an intravenous barbiturate.

that up and down the country interest in the method is increasing. I would make a serious plea that at least it should be considered in all patients mentioned above, in those with diabetes or other medical disorders and particularly when it is important to give the premature child every chance of survival. It is the anæsthetic which promises the normal and therefore the best oxygen supply in the mother's blood so long as the baby is dependent on the placental circulation.

For many years now, as a result of certain fœtal misfortunes, I have given no pre-operative sedative. Some received morphia ¼ grain at the beginning of infiltration, others receive nothing at all. On the other hand in order to ameliorate some of the rigours of local and to speed closure of uterus and abdominal incision I have someone give a little pentothal just before I incise the uterus. So far I have seen no harm result to mother or child and the patient is usually awake when the dressing is being applied. The specific advantages of local have been set out so well and so often by De Lee, Greenhill and others that I shall not repeat them here. There is only one word of warning and it concerns a technical point. When dealing with an uncorrected transverse presentation, never open the lower segment under local alone. The back, or the shoulder and an arm fall into the wound, and extraction may be almost impossible.

We are probably all agreed that in the present-day tendency to abolish all or most of the pain of childbirth there arise certain dangers for both mother and child. After all, and this is too often forgotten, the expectant mother is on the whole a most reasonable person. With simple and honest explanations her confidence can be won and she will no longer insist that safe delivery, whether vaginal or abdominal, should be entirely free from pain or discomfort.

REFERENCES

ANDERSON, A. R. (1946) *J. Obstet. & Gynec.*, **53**, 347.
BROWN, A. E. (1946) *Med. J. Aust.*, **2**, 488.
HARTZELL, C. H., and MININGER, E. P. (1946) *Surg. Gynec. Obstet.*, **82**, 427.
MENDELSON, C. L. (1946) *Amer. J. Obstet. Gynec.*, **52**, 191.

Dr. Katherine Lloyd-Williams; I propose to refer to the records of 305 cases done over a period of several years in the Obstetrical Department of the Royal Free Hospital. They fall into a pre-war series of 224 between 1931–39, and a post-war series of 81. During the war most midwifery was transferred from London, the Obstetrical Unit of the Royal Free was scattered, and though I was able to give the anæsthetics for Cæsarean section on many occasions at some of the outlying hospitals, I have no such full and continuous records of cases done in the war period.

TABLE I.—1931-1939. ANÆSTHETICS USED IN 224 CASES OF CÆSAREAN SECTION

Spinals:		
Stovaine 10%	10	85
Nupercaine 1 : 2,000	75	
Chloroform→ether		22
Ethyl cloride→ether		71
Gas and oxygen + some other anæsthetic (ether, vinyl ether, trilene, chloroform, evipan)		43
Cyclopropane		3

There were no maternal deaths.

TABLE II.—1945-46. 81 CASES (50 CLASSICAL C.S., 31 LOWER SEGMENT)

Anæsthetics used:	
Intravenous pentothal, gas and oxygen + trilene or ether	78
Caudal block	1
Local anæsthetics	2

There were no maternal deaths.

Infant mortality:
1945: No stillbirths.
2 died within twenty-four hours (1 atelectasis, 1 due to cerebral congestion from tight cord round neck. C.S. for fœtal distress).
1946: 1 stillbirth. Mother diabetic. Child probably dead before operation.
3 died within twenty-four hours—all atelectasis (1 premature).

I will describe briefly the methods I used from 1928 onwards and what caused me to modify these methods.

In common with many of my generation I had no experience, when I qualified, of chloroform anæsthesia beyond the occasional few drops on a mask in the maternity wards

Table III.—Cæsarean Sections 1944-1945-1946. Classification According to Anæsthetic

	G.O.E.	Epidural	Local	G.O.V.E.	G.O.T.	G.O.C.	Spinal
Disproportion ..	28 (1 N.D.)	2	6	2			
Placenta prævia ..	9 (1 N.D.)	4	2		1 (1 N.D.)		
Toxæmia	8	6	8			1 (1 N.D.)	
Diabetes	2 (1 N.D.)		3 (2 N.D.)				
Eld. primip. ..	9 (1 N.D.)						1
Heart, lung ..	7	1					
Miscellaneous ..	31 (1 M.D.)	7	4	2			
	94 (1 M.D. 4 N.D.)	20	23 (2 N.D.)	4	1 (1 N.D.)	1 (1 N.D.)	1

stand the operation without further anæsthetic, and of the remaining 63%, one-third had to have a general anæsthetic from the start and two-thirds received it as soon as the baby was born.

If those cases where a planned Cæsarean was done—cases of disproportion and of elderly primiparæ with complications—are extracted from the table, the neonatal death-rate is 4·2%. The neonatal mortality for normal labour is 2·45%. It seems extraordinary that a presumably healthy fœtus cannot be extracted from the mother without incurring mortality which is twice as great. This is of course an exaggeration as there are other factors to be taken into account but there is no doubt that the mortality is much greater than it should be.

It will be seen from Table III that the best results are obtained with epidural analgesia and I would like to describe this in some detail.

Premedication has been two doses of 100 mg. of pethedine, one one and a half hours before and the second three-quarters of an hour before operation, given intramuscularly. We have found pethedine of great value in all cases for allaying mental anxiety, and we have noticed no adverse effect on the infant, nor more than a tachycardia in the mother. However, if fœtal distress were present it would be wiser to forgo the pethedine.

We have always explained the procedure simply to the mother, making clear to her the difference between touch and pain.

Pre-operative use of pressor drugs has been omitted in patients with blood-pressure of 150 mm.Hg and over and has not been given routinely unless the blood-pressure has shown a tendency to fall.

Technique.—The patient lies on her side with her spine flexed. The skin is thoroughly cleansed with triple dye and an intradermal wheal of 1% novocain raised between L.2 and L.3, because the epidural space is widest at this level and the cord is not likely to be damaged. The Howard Jones spinal needle is inserted in the mid-line. Odom's glass indicator containing an air bubble is attached and then the needle is very slowly advanced through the ligamentum flavum until the air bubble is sucked in towards the patient by the negative pressure in the epidural space. If no negative pressure is observed another space may be tried.

We use 1 in 600 nupercaine in 0·45 normal saline, 45 c.c. in all, 10 c.c. of which is injected slowly, aspirating several times during its introduction, to make sure that C.S.F. is not being withdrawn. A wait of five minutes is now made in order to make sure again that the subarachnoid space has not been entered. If it has, C.S.F., which is warm, will drip out and a low spinal block will have occurred and voluntary movement of the toes will be impossible. Voluntary movements are not affected by epidural technique.

Following this safety pause, a further 35 c.c. of nupercaine are injected slowly (always aspirating several times and asking the patient to move her toes). This is well within the maximum dose and we have seen no toxic effects. The needle is then removed and the site of the puncture covered with elastoplast, and the patient lies on her back at a slight foot-down tilt while the analgesic solution is acting.

This usually takes twenty-five minutes and the surgeon must be discouraged from starting before this, otherwise the confidence of the patient is lost. With this dosage analgesia reaches approximately to D.8-D.10.

Those who definitely asked to go to sleep were given light supplementary gas and oxygen anæsthesia. Blood-pressure was taken continuously and several cases required no ephe-

The routine method is now:

Hyoscine 1/200 grain one hour pre-operatively. Pentothal combined with gas and oxygen, the intravenous injection not being given until the obstetrician is really ready to start. This is usually sufficient for the delivery of the baby. Omnopon 1/3 grain intravenously after delivery. This helps to reduce the respiratory excursion.

The operation is then completed with a further dose of pentothal if necessary or alternatively with the addition to the gas and oxygen of trilene, vinyl or ethyl ether in minimal amounts. With this method the baby more often than not cries immediately on delivery.

Post-operative anæsthetic complications seldom occur after Cæsarean section and there is indeed no reason why they should, for the amount of anæsthetic used is usually small, profound anæsthesia not being required. There were no complication in this series (Table II). In the 1931–39 series there was one case of lobar pneumonia occurring after the administration of chloroform–ether, and one disastrous case of an empyema and lung abscess which required rib resection. This occurred in an elderly woman (43) suffering from asthma and chronic bronchitis. A spinal puncture was attempted and failed and the anæsthetic given was gas and oxygen + chloroform and ether.

With the introduction of the intravenous barbiturates (and now curare and myanesin) there seems to me little reason for procedures which involve apprehension or mental strain for the patient. As I grow older, I ask myself before giving an anæsthetic: "Would I like it myself?" As far as spinals are concerned—or locals (which I admit for the special case are admirable)—my answer is "No".

Dr. C. J. Massey Dawkins: Every known method of anæsthesia has its advocates, but perhaps the fairest way of considering the matter is to look at it from the viewpoint of the consumers—which is the best anæsthetic for the mother and the fœtus? A search of the literature has revealed only one large series of cases where the results are tabulated according to the anæsthetic used, I refer to that published by Irving of Boston (Table I). In this table open ether carries off the honours, if the very small number of cases done under avertin are excluded. Table II, a series from the Obstetric Department of University College Hospital, shows that although the neonatal death-rate is about the same as the American series, the maternal mortality is considerably less. In Table III these figures are classified according to the anæsthetic used. For the last eighteen months we have ceased to operate on patients with diabetes, so that the neonatal mortality is now considerably less. Gas-oxygen-ether was used more often than any other anæsthetic but 46% of the babies required lobeline and carbon-dioxide and oxygen before they consented to breathe. This fact is a source of great strain to the surgeon and anæsthetist, the latter often has to leave his patient to resuscitate the baby and this form of anæsthesia should be condemned on this account. The maternal death was due to paralytic ileus which may of course occur with any operation. Local anæsthesia has not been entirely successful, only 37% of the patients being able to

TABLE I.—ANALYSIS OF 1,887 CÆSAREAN SECTIONS [1]

	G.Q.E.	Spinal	Open ether	Local	Cyclo.	Ether + O_2	Vinyl ether	Pento.	Avertin
Cases ..	948	261	195	170	141	77	63	25	7
Fœtal mortality	5·4%	4·0%	2·9%	9·7%	3·4%	6·0%	3·4%	5·0%	0·0%

Maternal mortality 24 = 1·3%

TABLE II.—CÆSAREAN SECTIONS 1944-1945-1946
(UNIVERSITY COLLEGE HOSPITAL, OBSTETRIC UNIT)

Disproportion	38	1 Neonatal death	
Placenta prævia	16	2 Neonatal deaths	
Toxæmia	23	1 Neonatal death	
Diabetes	5	3 Neonatal deaths	
Elderly primiparæ	10	1 Neonatal death	
Heart and lung disease ..	8		
Miscellaneous	44		*1 Maternal death*
	144	*8 N.D. (5·55%)*	*1 M.D. (0·69%)*

from the fœtal point of view. It is unfortunate that all inhalation anæsthetics seem to be transplacental and to affect the fœtus to a greater or lesser extent. This is shown by the fact that the fœtus so frequently shows a disinclination to breathe properly or cry for some time after delivery. If one does give an inhalation anæsthetic I maintain that the least amount possible should be given for the shortest possible time before the fœtus is delivered. Some surgeons request a fairly deep anæsthetic from the start and then later proceed to harass the anæsthetist with inquiries as to why the infant is not crying.

Of the 13 inhalation anæsthetics, 4 children cried spontaneously within five seconds and the rest showed some difficulty for five to ten minutes. Of the 15 spinals, 14 cried as soon as the head was free; one was difficult for five minutes and this we felt was due to the fact that the mother was operated on as an emergency and had been dosed with morphia before coming into hospital.

Let us now look at the maternal point of view. Spinal anæsthesia is a recognized technique which, despite a considerable amount of controversy, has stood the test of time and is still recognized as a legitimate procedure in reasonably competent hands. I can see no reason why it should not be used for a Cæsarean section just as adequately as for the relief of any other abdominal tumour. I have found that when it is explained to patients that spinal anæsthesia would avoid a risk of poisoning the child they have been anxious to have it. Furthermore they seem to find much pleasure in hearing the infant cry as it is delivered, and those who have had previous children normally have usually been very pleased with the results of spinal anæsthesia.

Perhaps I may be allowed to trespass a little and discuss the effects of the spinal on the operation itself as seen from my end of the table. Anæsthetists must, of necessity, as a result of their peculiar position with regard to surgery, become very censorious critics of surgeons and surgical procedures. As I see it the surgeon must make one of two choices: if an inhalation anæsthetic is being given, he must either proceed in his normal way, tying off his bleeding points as he goes, regardless of the effects of the anæsthetic on the fœtus, or else he must proceed at a rate far in excess of his normal, which he is probably very reluctant to do; on the other hand, with a spinal, he can proceed at whatever pace he likes, safe in the knowledge that the fœtus is not being affected. Furthermore, he has a degree of muscular relaxation greater than which not even the most pernickety surgeon could require and which could only be got with a very considerable quantity of inhalation anæsthetic. The delivery of the fœtus is usually uneventful although I admit—and here I must make it clear that in general I am speaking of the lower segment operation—I have seen one case in which the contraction of the uterus made the delivery of a large head very difficult. There is usually a quick and spontaneous expulsion of the placenta and the uterus remains hard. So far, I have not seen any post-partum hæmorrhage following a spinal but I have seen considerable trouble with the uterus in three out of 13 patients who had inhalation anæsthetics, although in every case I endeavoured to keep the inhalation anæsthetic to a minimum commensurate with a reasonably satisfied surgeon.

To sum up: from my own experience I feel that when there is no contra-indication to its use, a spinal anæsthetic is one of those which gives the best chance of a live child and the minimum risk of post-partum hæmorrhage.

Mr. Linton Snaith: For the past four or five years I have been using local anæsthetic for practically all Cæsarean sections, supplemented frequently by pentothal or cyclopropane or gas and oxygen given usually after the uterus has been opened, but with negligible premedication. My experience covers between two and three hundred cases operated on personally and another hundred or so in which other members of the staff of my department were concerned. I am satisfied with the method, though I must admit that I fall short of the standard of local anæsthesia described by Mr. Marshall. In a number of cases, however, I have had the experience of delivering the baby and having it breathe and cry immediately, often before complete removal from the uterus, only to relapse into a condition of collapse not far short of white asphyxia. None of these babies have died, but they have given rise to anxiety and have required some artificial resuscitation, and I would like to know the reason. This has occurred in cases where there could not possibly be any depressing effects from general anæsthetic or from premedication, and I would emphasize that the child has in such cases shown activity and spontaneous respiratory effort before its relapse. It seems that not even local anæsthetic removes all risk of trouble with the baby and it may be that where similar trouble occurs under general or spinal anæsthesia the anæsthetic is unneccessarily blamed.

drine at all. All the babies breathed spontaneously at birth. There were no headaches, chest complications, or urinary troubles. Vomiting was almost negligible. Relaxation of the abdominal muscles was good. Retraction of the uterus was satisfactory and there were no cases of post-partum hæmorrhage.

Many have been deterred from using this method owing to technical difficulty and occasional failures but I think the results justify the trouble involved.

I quote the opinion of one of the ward sisters at U.C.H. [2] who has nursed a great number of Cæsarean sections: "The patients return to the ward conscious and are most co-operative. They are calm, and quiet, compared with the restlessness following general anæsthesia, and do not complain of thirst and are free from pain. As a rule their general condition is better than with other anæsthetics, and they do not vomit. Very soon after operation they are able to take light but solid food and hence are much less likely to get discomfort from flatulence. The amount of post-operative drugs required is much less than with general anæsthesia. The impression of the nursing staff is in favour of epidural analgesia for Cæsarean sections."

Epidural block has many advantages over spinal analgesia. There is no risk of meningitis or nerve palsies, the fall in blood-pressure is much less, and there is no headache. I inquired from a ward sister of a provincial hospital where spinal analgesia is given as a routine, as to the condition of the patients after operation, and the reply was to the effect that the majority suffered from severe headaches owing to the haste with which they were elevated to Fowler's position. I have yet to meet an anæsthetist who would choose to have a spinal himself.

In conclusion I should like to say that an anæsthetist who cannot produce a baby which cries immediately on delivery has failed in his duty towards his patient.

REFERENCES

1 Irving, F. C. (1945) *Amer. J. Obstet. Gynec.*, **50**, 660.
2 Crouch, D. M. E., and Merry, E. S. M. (1946) *Brit. J. Anæs.*, **20**, 24.

Dr. J. N. Cave: I have perhaps been biased in favour of spinal anæsthetics in consequence of my early contact with Dr. Clement Norman of Broadstone, who is one of their great exponents. Subsequent experience has, however, left me convinced that they are among the best anæsthetics for Cæsarean section.

As all anæsthetists here will probably agree, although one may have considerable convictions about the suitability of a method of anæsthesia we are often hampered by the quite strong prejudices of surgeons. I venture to say that anæsthetists, perhaps because they have more than one card to play, are usually the more adaptable and so one cannot always pursue a line of inquiry as far as one would like, especially as it is obviously undesirable to have a surgeon operate in a disgruntled state of mind.

Since demobilization last year I have given anæsthetics for 28 Cæsarean sections. Of these 15 have been spinals, 12 inhalation and 1 a local going on to an inhalation. Of the 12 inhalations 7 were given for a variety of surgeons who expressed either a strong prejudice against spinals or expressed a strong wish for an inhalation anæsthetic.

The remaining 21 anæsthetics were all given for the same surgeon—of these 15 were spinals, 5 were inhalations, 1 was the mixture of local and inhalation. Of these 6 inhalation anæsthetics, 2 were given because the situation was obscure and examination under an anæsthetic was necessary before deciding on surgical interference. As in such cases the odds are slightly against the Cæsarean being required it did not seem justifiable to give a spinal. Two were given because the patients insisted on being put to sleep—and one because a patient became hysterical when the lumbar puncture was being made. The mixture of local and general was for a patient who was sent in as an emergency and was in poor shape when she reached the theatre—obviously a bad subject for a spinal. Local was used until the uterus was reached, gas and oxygen and a small amount of ether for the delivery of the child and final sewing up.

In the majority of cases the object of a Cæsarean section is to produce a live child; if the life of the mother were the only consideration the child could, by one means or another, be removed by what one might call the usual channels. So let us examine the results first of all

Section of Ophthalmology

President—HAROLD LEVY, F.R.C.S.

[*February* 13, 1947]

The following cases were shown:—

Familial Dystrophy of Cornea.—P. G. DOYNE, F.R.C.S.

Arteritis of the Temporal Vessels Associated with Loss of Vision.—SIMON BEHRMAN, M.R.C.P.

Persistent Pupillary Membrane Showing a Network Pattern.—HOWARD REED, D.O.M.S., for Professor ARNOLD SORSBY, F.R.C.S.

Mooren's Ulcer.—M. LEDERMAN, M.B., and A. RUGG-GUNN, F.R.C.S.

Melanotic Sarcoma.—P. GARDINER, M.B., for T. KEITH LYLE, F.R.C.S.

Denig's Operation for Trachoma (Two Cases).—NOAH PINES, M.B.

Mooren's Ulcer.—Professor B. W. WINDEYER, F.R.C.S.Ed.

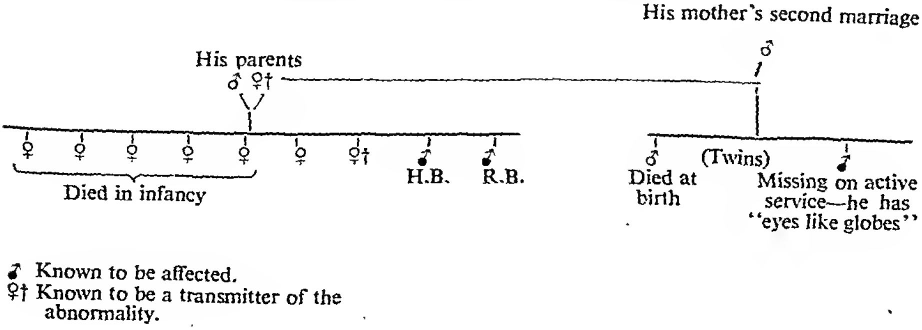
Devicz's Disease.—A. S. PHILPS, F.R.C.S.

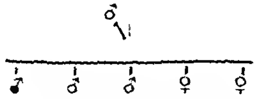
Retinal Glioma (Three Cases).—Professor B. W. WINDEYER, F.R.C.S.Ed.

Bilateral Embolus of Central Retinal Artery.—C. L. GIMBLETT, F.R.C.S.

Megalocornea (H.B., *see* Table)—H. E. HOBBS, F.R.C.S.

GENEALOGICAL TABLE OF H. B.'S FAMILY


His mother's second marriage
His parents
♂ ♀†
♂
♀ ♀ ♀ ♀ ♀ ♀ ♀† ♂ ♂
H.B.
R.B.
Died in infancy
♂ (Twins) ♂
Died at birth
Missing on active service—he has "eyes like globes"
♂ Known to be affected.
♀† Known to be a transmitter of the abnormality.



The eldest son of the only married sister is said to have "eyes like globes"

Mr. H. J. Malkin gave a preliminary report on 767 consecutive cases of Cæsarean section performed by his colleagues and himself during the last eight years at the City and Women's Hospitals, Nottingham. Of these, 736 were done under spinal anæsthesia, for which light duracaine was used almost entirely. This series covered all types of cases, including set and emergency operations for contracted pelvis, cardiac disease, toxæmia, placenta prævia, diabetes, &c.

There were eight fatalities, the causes of death being as follows:—

Pulmonary embolism ..	19th day	1
Peritonitis	6th day	1
Diabetic coma	12 hours	1
Hypertension, cerebral hæmorrhage	2 hours	1
Hæmorrhage from extra-uterine implantation of placenta ..	2 hours	1
Lobar pneumonia	9th day	1
Intestinal obstruction, previous Cæsarean section and multiple adhesions	2nd day	1
Staphylococcal septicæmia following breast abscess ..	12th day	1

It appeared that no fatality could be attributed to the spinal anæsthetic *per se*.

Among the earlier cases there were some which gave anxiety during the operation, but modification of technique had reduced these to a minimum. The modifications were: (1) reduction of the dose, (2) reduction of the time during which the patient is turned over on to her abdomen, and (3) the giving of a vasopressor substance. The turning of a pregnant patient on to her abdomen was a drawback to the method, but could be met by adequate support to the chest, and if necessary the pelvis, by pillows; this drawback did not apply to heavy nupercaine.

Mr. Malkin thought that absence of premedication had an unfavourable effect on some cases, and he had found that preliminary pethedine and hyoscine, as mentioned by Haultain, or chloral, was of great assistance. He expressed his thanks to his colleagues, Miss Glen Bott and Miss Bates, for allowing him to include their cases in the series, and to Dr. Cochrane and Mrs. Marrow for their considerable help in the collection of the records.

Dr. J. B. Cochrane (City Hospital, Nottingham), who had performed a considerable number of Cæsarean sections in the series referred to above, gave details of the technique of administration of the anæsthetic. The method employed consisted in giving 1·4 c.c. of light duracaine, turning the patient over for one minute only, and the intramuscular administration of 30 mg. of methedrine when the spinal anæsthetic was inserted. He felt that with this technique, light spinal duracaine gave no cause for anxiety in Cæsarean section.

Hence one is naturally loth to apply any form of caustic to the ulcer which might conceivably give rise to a nebula, and although each individual attack clears up in a variable time with simple treatment—the milder ones even doing so spontaneously—recurrences are very difficult to check.

In some cases the attacks may continue in a milder form after a course of treatment, and a further course after a suitable interval may be required.

In superficial punctate keratitis, an obstinate condition, about half my cases have benefited from radiotherapy; this is a condition which, as I think most will agree, does not respond readily to other methods of treatment.

I am sure that my results warrant my saying that the treatment is well worth a trial in any given case.

The ætiology of superficial punctate keratitis is admittedly obscure, different cases show varying clinical characteristics, and it may well be that they are not all of the same nature. Some of my successful cases had a history of long duration, and in those especially the cures were most gratifying.

Phlyctenular keratitis bears some resemblance clinically to acne-rosacea keratitis, in that the corneal lesions occur initially as infiltrates. But the exacerbations of this disease respond as a rule readily to other methods of treatment, and I have not found it necessary to resort to radiotherapy except in a few obstinate cases, which responded well.

My views on the effect of mild radiotherapy in cases of spring catarrh are as follows:

Severe cases with gross vegetations covering the palpebral conjunctiva, in whom the disease is present throughout the year and merely exacerbates during the spring and summer, show no encouraging results with mild radiotherapy. But in the mild cases whose eyelids are normal during the winter months, and who show fresh manifestations in the early part of each year, the treatment is well worth a trial.

If applied immediately when any signs of recurrence become evident, it may check further developments. I may emphasize here that I am dealing only with a mild dosage.

In the treatment of other types of corneal ulcer, including Mooren's ulcer and dendritic ulcer, I have not had any success with this method. Nor have I found it of value for any form of deep keratitis.

I must admit, however, that owing to my unpromising initial results—so different from those obtained in the rosacea cases—I was not encouraged to proceed further with the treatment of such conditions.

Professor B. W. Windeyer: A cardinal principle in the radiotherapy of malignant disease of the eye is to avoid or shield the eye itself whenever possible, owing to the danger of permanent damage resulting from even moderate dosage.

The most common sequelæ are those associated with the lids and lacrimal apparatus, the conjunctiva and the lens. Scarring of the lids may cause entropion or ectropion and closure of the punctum by scar tissue may result in persistent epiphora. Heavy irradiation of the conjunctiva may be followed by chronic conjunctivitis with some loss of sensitivity and chronic irritability. In such cases vascular changes are usually apparent; microscopically there is degeneration of the arterial vascular endothelium, followed by regenerative hyperplasia with narrowing of the lumen of the vessels and, clinically, dilatation of superficial capillaries and permanent telangiectasis occur.

The changes which occur in the lens after irradiation have been studied by various workers. As a rule no immediate change is seen in the function or appearance of the lens even after exposure to heavy dosage and in the great majority of cases the lens remains apparently perfectly healthy. At a later date, however, there may be degeneration of the lens with the formation of cataract and this is probably the most common late sequela of irradiation of the eye. The radiosensitivity of the lens as determined by liability to cataract formation varies greatly in different individuals. In some cases after exposure of the eye to very heavy dosage, for example in the treatment of malignant tumours, there has been no demonstrable effect, even many years later. In others with more moderate dosage, usually after the lapse of several years, progressive cataract formation has been observed. It is probable that radiation cataract is more likely to occur in those who are debilitated and undernourished, in young children and in elderly people with a tendency to spontaneous cataract formation, but it has also been found in healthy young adults. The quality of the radiation, whether hard or soft, does not seem to be a determining factor, and there would appear to be some danger of cataract formation with any dosage level which causes a definite conjunctival reaction.

DISCUSSION ON RADIOTHERAPY IN THE TREATMENT OF NON-MALIGNANT SUPERFICIAL EYE LESIONS

Mr. R. Affleck Greeves: I propose to deal solely with the treatment of superficial corneal lesions by means of mild sub-erythematous radiotherapeutic doses, with an additional brief reference to spring catarrh treated by the same method.

The possibility of treating corneal lesions by this method first occurred to me eighteen years ago in connexion with cases of acne-rosacea keratitis.

In the course of my routine out-patient hospital work, a number of these distressing cases appeared from time to time; the condition is, as a rule, extremely resistant to ordinary methods of treatment.

While, in my experience, it is not uncommon for the corneal complications to develop late in the disease, at a stage when improvement may have already taken place in the skin condition, one also meets with cases in which both types of lesion are present. I was in the habit of sending such cases to my colleague, Dr. MacCormac, for dermatological treatment, and, struck by the great improvement in the skin lesions resulting from radiotherapy, it occurred to me that it might be possible to apply the same measures to the cornea.

In conjunction with my colleague, Dr. Douglas Webster, I therefore explored the literature dealing with the results of experimental application of X-rays and radium to the eyes of animals with a view to determine if possible a dosage which would undoubtedly be free from any harmful effects. By this means we arrived at the decision that what was known in those days as a third of a pastille dose would be perfectly safe. The dose actually given was smaller than this.

Many chronic cases which had been coming to Out-patients week by week, with mournful regularity, improved rapidly with this treatment and ceased to attend.

The eyes whitened, infiltrates were replaced by healing scars and pain and photophobia vanished. On the whole the results were excellent and the majority of my cases reacted most favourably. But in line with one's common experience of therapeutic measures in general, there is always a tiresome minority of obstinate cases, which do not respond so well or so quickly, and this method is no exception to the rule.

I do not claim that radiotherapy for acne keratitis cures the condition. Its underlying constitutional cause is obscure and it is therefore obvious that until further knowledge has been gained, so that suitable general treatment directed towards removing the cause of the disease can be instituted, local manifestations are almost bound to recur.

I am convinced, however, that the periodic exacerbations can be checked in most cases by means of radiotherapy, expecially if this is given at an early stage.

The exacerbations are especially prone to occur in spring or early summer, a fact which suggests that sunlight may have a provocative effect. They take the form of an infiltrate, in the superficial layers of the cornea associated with pain, photophobia, and lacrimation; this infiltrate breaks down and becomes an obstinate and chronic corneal ulcer, and is ultimately replaced by scar tissue which forms a fairly dense nebula.

Before I instituted the treatment, these cases dragged on for weeks or even months in misery, but when treated their improvement was rapid, and after two or three weeks, disappeared, only to turn up again in the following spring with a fresh attack. But these fresh attacks yielded rapidly to the treatment, and the patient again disappeared until the following year, or in some cases after a much longer interval, when they again demanded that the treatment should be repeated.

Encouraged by my results in acne-rosacea keratitis, I tried the treatment in other corneal diseases.

It has proved to be markedly beneficial in recurrent abrasion and superficial punctate keratitis. In cases of recurrent abrasion it is, I think, especially useful. Here the ulceration is usually limited to the corneal epithelial layer and therefore heals without leaving any scar.

lasting for one or two days, but in the majority there has been no appreciable reaction and a rapid subjective and objective improvement has occurred.

The cases have been confined almost entirely to acne-rosacea keratitis, recurrent abrasions and erosions, and superficial punctate keratitis of the multiple erosion type. With this group of cases it is not possible to give a statement of results based on a definite statistical analysis as they have not been followed routinely with this end in view. Even without routine follow up it has been possible however to be sure of certain conclusions.

The cases of acne-rosacea keratitis appear to give the most gratifying results, as practically all of them get marked subjective improvement and rapid healing of individual exacerbations of the disease. They do recur at varying intervals, but the patients recognize that they have derived such benefit that they usually come for treatment again early in an attack which can be cut short in the majority of cases and may not need a full treatment.

Recurrent erosions and abrasions also respond with rapidity and although recurrence may occur after X-ray therapy it is not so frequent nor of such severity when the patient comes again for treatment. Many have remained healed with no recurrence after a single cross-fire treatment.

Cases of superficial punctate keratitis of the multiple erosion type have been the largest single group in our series and at least half the cases have shown a satisfactory response. Some have shown the same tendency to recurrence as the cases of acne-rosacea keratitis and have received up to six treatments over periods up to four years, showing improvement after each treatment similar to the acne-rosacea cases. Others have had one or two treatments spread over one to three months with relief of symptoms. The outstanding impression gained from a study of these groups of cases, acne-rosacea keratitis, recurrent erosions and superficial punctate keratitis was that X-ray treatment had often succeeded after other methods of treatment had failed or had only produced some temporary alleviation and that, while many cases did recur after X-ray therapy and needed a further course of treatment, they tended to be free of symptoms in the intervening period and did not have to make frequent attendances for local applications, as many of them had done previously.

My experience of other superficial non-malignant conditions of the eye has been much more limited. In Mooren's ulcer this technique has not been found to be effective and for the last three or four cases which have been treated the dose has been increased using the same cross-fire arrangement of fields. The patient shown to-day, a young woman, was first treated by the actual cautery in June 1945. In July and August 1945 she was given 1,200 r to both medial and lateral fields over a period of twenty-eight days. At the end of treatment there was definite improvement and the ulcer was healed either on account of or in spite of this treatment within six weeks. I have had no experience of the treatment of these lesions with radium applicators with either β or γ radiation.

In spring catarrh the results on the whole have been disappointing. We have not thought that it was justifiable to give heavy dosage which might cause permanent scarring and chronic conjunctivitis for a condition which is ultimately self-limiting. We have employed milder dosage, either by everting the lids and applying a lightly screened β ray radon applicator or by irradiating with X-rays, through the closed lid after cocainization of the conjunctiva and the insertion of a lead screen to protect the eye. Doses of the order of 150 r have been given in this way with X-rays generated at 95 kv. with 1 mm. aluminium filter and have been repeated at intervals of two to three weeks up to four treatments. There has been only slight response when treatment is given during an exacerbation in the spring or summer, but there seems to be definite benefit to be derived from giving such a course of treatment towards the end of the winter before the eyelids begin to be inflamed again. In some mild cases the seasonal attacks are almost aborted and in others their severity is reduced.

Dr. M. Lederman: Although radiotherapy is now accepted as a therapeutic agent of value in many specialities, in ophthalmology it has not yet received the recognition it merits.

The reasons for this are twofold: (1) Current misconceptions concerning the susceptibility of the eye to radiation damage; (2) the eye diseases for which radiotherapy is suitable are not common, hence its field of usefulness is rather restricted.

The view that the eye is readily damaged by radiation cannot now be supported, as it is largely based upon early, unscientific experimental work, and the ocular disasters encountered by pioneer radiotherapists. With modern apparatus and technique, damage to the eye is avoidable when treating non-malignant lesions; risk of ocular damage has to be accepted only when treating malignant neoplasms which affect the eye or its neighbouring structures.

Philippa Martin, who has made a study of injury to the eye by therapeutic radiation, gives two years or even longer as the period likely to elapse between the time of the treatment and the onset of cataract. She has, however, observed the early occurrence of cataract; in one case it appeared three days afer the irradiation of the eye and was mature after the lapse of seven weeks, while in another case of which the lens showed vacuolation ten days after treatment, the vacuoles had disappeared after fourteen weeks. Colwell and Russ state that the earliest recorded time for cataract to appear is four months after irradiation.

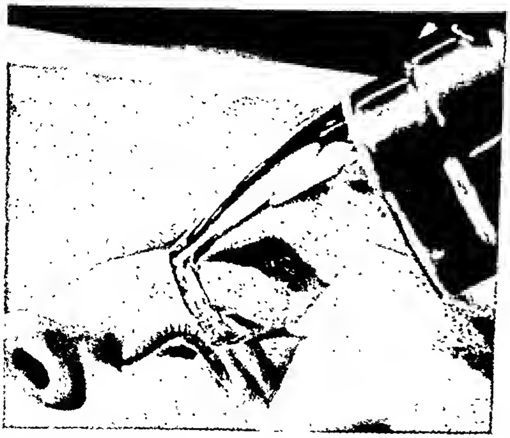
The typical irradiation cataract is posterior cortical with radiating rows of vacuoles and these may be arrested in the vacuolar stage or may go on to maturity, vacuolar opacities gradually becoming scattered through the entire lens cortex, which eventually becomes completely opaque. A mature irradiation cataract shows no special clinical features and responds as well to operative treatment as do other forms of cataract.

While cataract formation is not an uncommon sequel of irradiation it must not be forgotten that cataracts do form in elderly people without previous irradiation, and that every case of cataract in people who have been irradiated is not necessarily due to this cause.

Many other rarer sequelæ of irradiation of the eye have been described but these recapitulated here are the commonest and might occur perhaps without excessive dosage.

The technique which has been used at the Middlesex Hospital for the treatment of superficial non-malignant conditions of the eye has been designed to avoid these dangers both by the direction of the beam to avoid the lens and by limiting the dose delivered to one which has been shown to be well tolerated and insufficient to cause any damage.

In 1937, Dr. Douglas Webster described the technique which he had worked out with Mr. Affleck Greeves for the treatment of superficial corneal lesions by cross-firing the cornea with X-ray beams. This technique, with very minor modifications, has been used continuously from 1926 up to the present time. The technical factors are as follows: X-rays generated at 95 kilovolts; 1 mm. aluminium filter; 2·5 milliamperes current; 18 cm. focal skin distance.



The cornea is irradiated from the lateral (*see* fig.)—and the medial sides, using a beam which is sharply defined by means of a lead glass applicator with a 2·5 cm. diameter aperture. The tube is arranged for each field so that the lower margin of the beam only is directed across the cornea and irradiation of the lens is avoided. but the whole of the surface of the cornea is irradiated.

The patient is treated with the eye open and is instructed to look fixedly at a white mark which is placed in a suitable position on the X-ray tube housing. This produces sufficient fixation of the eye with slight internal rotation for the lateral field and external rotation for the medial field. The setting of the tube for each treatment, which is invariably carried out by one of the radiotherapists and never by a technician, has to be undertaken with great care, especially the medial field where the applicator comes in contact with the patient's nose.

A dose of 100 r measured at the aperture of the applicator is delivered to each field. Taking into consideration the distance from the end of applicator to the centre of the cornea, which is calculated as 1·8 cm. and the fact that the extreme edge of the beam is used, it is estimated that the cornea receives a dose of 60 to 65 r from each field or a total of 120 to 130 r per treatment. With the factors stated the treatment of each field takes less than two minutes. This dose is repeated if necessary at fortnightly intervals, up to a maximum of four treatments in a single course. Some patients have had the course of treatment repeated several times at intervals of nine months to a year or more.

Webster reported the treatment of 146 patients with superficial corneal lesions treated between 1926 and 1936 and since that time a further 108 patients have been treated, a total of 254. The numbers were smaller during the war years. There has not been any evidence of late damage in these cases. In some cases there has been an exacerbation of symptoms

The dosage required is important since: (1) Improper dosage may aggravate the condition: (2) repeated treatments for recurrent attacks may become necessary, and without proper care can be dangerous.

My first cases of superficial punctate keratitis and rosacea keratitis were treated by superficial X-ray therapy, the technical factors being: 90 kV., 4 ma., 1 mm. Al filter, F.S.D. 23 cm. A field just large enough to fit between the margins of the bony orbit was used and treatment given directly through the closed lids. No special measures to protect the lids or lashes are necessary. Doses of the order of 70 to 100 r were given once a week for four to five weeks.

With these doses there may be an exacerbation of symptoms. In order to eliminate this possibility and also with a view to the probable need for repeated courses of treatment, in recent years I have been giving a minute initial dose, i.e. 10 to 15 r. I have noticed no difference in results by starting with this small dose and gradually increasing it to a final dose of 40 to 50 r, treatment being given twice a week. The initial "flare-up" is eliminated and the total dose required, about 200 to 250 r, is almost half that given by the earlier technique. Total doses of this order spread over four to five weeks can be safely repeated on a number of subsequent occasions if necessary. It is important to emphasize that a rigid standard technique is to be avoided and individualization of treatment is essential.

Miscellaneous conditions (Table III).—I have treated a few opacities with no striking results, although every now and then there does seem to be some improvement. I have also treated a few corneal dystrophies without much success. Although I have not had the opportunity of treating pterygium, the American literature contains quite definite claims for radiotherapy in the treatment of this condition.

Two of the remaining conditions, namely corneal ulceration and recurrent erosion, are most definitely favourably influenced by radiotherapy. A single dose of X-rays (75 r) will often act like magic on an erosion. Symptoms are relieved very quickly and only exceptionally is a second or third dose necessary.

In corneal ulceration, excluding Mooren's ulcer, X-ray therapy not only relieves symptoms but sometimes results in healing. The technique of treatment is approximately the same as that employed for superficial punctate keratitis and rosacea keratitis.

TABLE III.—MISCELLANEOUS CONDITIONS

Corneal ulcer, including Mooren's ulcer	*Degenerations and dystrophies*	Pterygium Cornea
Corneal opacities, following infection or trauma	*Traumatic lesions*	Recurrent erosion

Mooren's ulcer presents a special problem. Radiotherapy has frequently been advocated but its value has never been established. I have seen 6 cases, including 2 with bilateral lesions. Good results have been obtained in only two lesions, one has remained healed for two years four months, and the other for two years five months. In both cases treatment was given with a special beta-ray applicator (fig. 1). The remaining lesions treated by X-ray therapy were all failures.

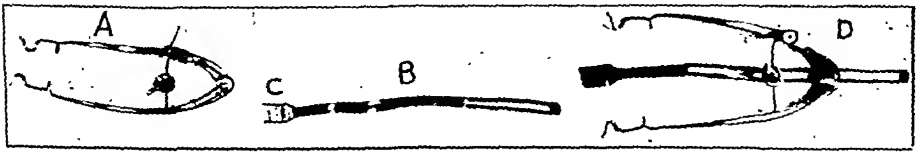


FIG. 1.—BETA-RAY APPLICATOR

A = Speculum with universal screw.

B = Radium spatula consisting of a malleable, slotted brass holder and C = A hinged radium applicator. The radium spatula can be used separately for lesions of the palpebral conjunctiva or lids.

D = Apparatus assembled for treatment of lesions of the cornea or bulbar conjunctiva.

Acknowledgments.—I am indebted to the members of the staff of the Royal London Ophthalmic Hospital and the Western Ophthalmic Hospital for referring cases for treatment and for permission to use the material thus obtained. I am particularly indebted to Mr. C. Dee Shapland, Ophthalmologist to the Royal Cancer Hospital, for helpful advice and criticism.

The beta-ray apparatus was made by Messrs. Down Brothers, and the radium applicator by Messrs. Johnson, Matthey & Co.

Three types of radiation can be used in the treatment of non-malignant lesions of the eye; the beta and gamma rays of radium and X-radiation. X-rays have largely replaced radium in ophthalmology because of technical simplicity, the ease with which the tissues not requiring treatment can be protected, and the short treatment times needed.

Nevertheless, radium still has its indications. Thus, beta radiation, using special applicators, offers advantages in the treatment of certain lesions of the cornea, limbus and conjunctiva. Similarly gamma radiation possesses certain advantages over X-radiation, in the treatment of hæmangiomata and keloids.

The non-malignant lesions for which radiotherapy can be used fall into three groups: (1) Benign tumours; (2) inflammatory lesions; (3) miscellaneous group.

The purpose and technique of treatment vary from group to group but the underlying principle of treatment is to give the smallest possible dose which will achieve the desired result.

Benign tumours.—Table I shows some of the commoner benign tumours encountered by the radiotherapist. Not all of them respond to radiotherapeutic treatment and it is of vital importance that cases be properly selected. When this is done the results of treatment are usually extremely gratifying, whereas indiscriminate treatment may be both harmful and dangerous.

The hæmangioma and the keloid are essentially the province of the radiotherapist whereas the pigmented tumours are best left alone or dealt with surgically. Solitary papillomata and hyperkeratoses can be treated quite adequately by radiotherapy, but where there is any doubt about their benign nature, excisional biopsy should be performed.

TABLE I.—BENIGN TUMOURS

Hæmangioma	Eyelids	*Hyperkeratosis*	
	Conjunctiva		
	Orbit	*Benign Melanoma* (Pigmented nævus)	Lids
Keloid			Conjunctiva
Papilloma	Lids		
	Conjunctiva		

With regard to *inflammatory lesions* one is on less certain ground. At some time or another radiotherapy has been tried in the treatment of most ocular inflammations. Whilst many of the claims made in the literature should be accepted with reserve, the fact does emerge that radiotherapy can be of use, particularly in the treatment of some of the more refractory inflammatory disorders.

Any indiscriminate or immediate resort to radiotherapy in the treatment of ocular inflammations is to be deprecated. Radiation is, after all, a noxious agent, its precise mode of action on inflammatory processes is still a matter for conjecture, its effects are by no means prompt, and in acute cases valuable time may be lost. When chemotherapeutic, surgical or other procedures are known to give satisfactory results, these should always be given priority.

Table II lists a number of conditions in the treatment of which I believe radiotherapy has a part to play.

Superficial punctate keratitis and rosacea keratitis are the two conditions of which I have had most experience and they can be considered together, as it is in their treatment that radiotherapy is neglected.

TABLE II.—INFLAMMATORY PROCESSES

Pyogenic	Blepharitis	*Virus*	Trachoma
			Herpes ophthalmicus
Granulomatous	Tuberculosis		Superficial punctate keratitis
	Sarcoidosis	*Unknown ætiology*	Rosacea keratitis
Allergic	Spring catarrh		
	Phlyctenular kerato-conjunctivitis		

Radiotherapy cannot cure all cases, but for the stubborn case much can be done by way of symptomatic relief and improvement of physical signs, and on occasion clinical cure can be achieved. There can, of course, be no guarantee against recurrence.

There is a very high percentage of bilateral lesions in this series—higher than is usually quoted in the literature.

Dr. N. S. Finzi said that he would like to discuss the cases just presented. Mr. Durden Smith had said that he gave 6,000 r of the beta radiation. It was necessary to point out that gamma radiation would not fall off in anything like the same degree per mm. of tissue as the beta radiation. How much of the results was due to the gamma radiation he would be able to tell in the future, because after a time he would be able to use radioactive isotopes, and Dr. Finzi thought that radioactive phosphorus would give beta rays only, so that it would be possible to see whether he could get the results with beta rays alone without the addition of gamma rays.

With regard to the other cases he agreed with what Professor Windeyer had said and with most of what Dr. Lederman had said. He did not agree that capillary angioma did not respond at all. He had occasionally got very good results in that condition. Professor Windeyer had made the actual measurements with his cases so that Mooren's ulcer did require more dosage, but when one was using the edge of the applicator it was very easy, especially with a lead-glass applicator, to get a little bit out and not to give quite the dose one thought one was giving. Therefore he might possibly have given rather smaller doses than he supposed, but Professor Windeyer was a very careful observer and it must be accepted that the doses he mentioned were actually given in these particular cases. With inflammatory conditions in general very small doses were required.

Mr. Eugene Wolff said that he had seen half a dozen cases of stenosis of the punctum and canaliculus after radiation. These cases were difficult to treat, and he wondered whether one ought not to slit the canaliculus in every case, before radiation.

Dr. B. Thorne-Thorne referred to a young girl, aged 6, who had dermolipoma of both eyes. In one eye there was now infiltration down over the cornea which seriously affected the vision. He wondered whether any form of radium or X-ray application was likely to bring about relief.

Professor Windeyer said, in reply to Dr. Finzi, that it was very difficult to be absolutely sure of the measurement, as a very small alteration in the accuracy of setting up might make a difference of as much as 50% to the dose received on the cornea, and it was likely that inaccuracies would decrease rather than increase the dose. Nevertheless, he felt reasonably confident that the dosage which he had described had been given.

On the question of scarring of the punctum (Mr. Wolff), this was a very serious thing in the treatment of certain malignant neoplasms, particularly basal-cell carcinoma around the lid, and it was a very distressing condition. He did not think that splitting of the canaliculus would get over the trouble, because in these cases, i.e. heavy doses for malignant disease, there was very marked scarring. He had not observed this to have occurred in the treatment of these non-malignant conditions in which they had given such small dosage. He did not think it a danger to worry about.

A dermolipoma (Dr. Thorne-Thorne) he thought unlikely to be radiosensitive.

Dr. M. Lederman, also in reply, referred to the dosage used with Mooren's ulcer. He himself had not used one consistent dose but had attempted to gain the maximum information. One unilateral case he had treated with small doses was an utter failure, and cases he had treated with doses almost approaching those used in malignant disease were equally a failure. In his two successful cases a single dose of 1,500 r was given using a special beta-ray applicator—the treatment time being about eleven minutes.

With regard to dermolipoma he would say on general principles that radiation was unlikely to help.

He reiterated what Professor Windeyer had said concerning the canaliculus.

Mr. A. J. Durden Smith: *Mooren's ulcer.*—Among non-malignant conditions affecting the eye Mooren's ulcer is outstanding for several reasons. It is a rare disease—the series I propose to examine amounts to only 42 cases and these have been treated at the Radium Institute over a period of fifteen to sixteen years. It is among the most distressing of eye conditions in that the symptoms—pain, epiphora and photophobia—are usually so marked as to reduce patients to a pitiable condition of mind. It is a form of corneal ulceration which is very difficult to cure and even when healing is achieved the results in terms of loss of vision are often deplorable, and depend in any case on the extent of the ulceration at the time of its first treatment.

Treatment.—Treatment has been uniform over a number of years, and Roy Ward of the Radium Institute in London did much of the early work on the subject. Contact radiation with unscreened radium applicators has been the method used, the applications being given as a rule three times at intervals of six weeks, whether the primary result is satisfactory or not.

Technique.—After cocainization the patient lies on a couch in the dorsal position with the head immobilized by sandbags. A speculum is inserted into the affected eye, and the radium applicator, covered by para-rubber and lubricated with liquid paraffin, is held in contact with the cornea. A piece of adhesive tape, previously applied to the applicator, is used to fix the latter to the cheek and eyebrow, and other pieces of tape are used, if necessary, to position the applicator accurately on the cornea. The room is then darkened and a dull red neon lamp on a stand and capable of movement in all directions is so adjusted that when the patient gazes at it with the sound eye the area of ulceration is beneath the applicator. This is done by the light of a stick lamp. The patient is warned that he must continue to gaze steadily at the lamp and he is inspected at frequent intervals to see that he is doing so, and that the applicator remains in position. Treatment time is usually in the region of an hour. A good deal of concentration on the part of the patient is required for this, and one gets the impression that the best results are obtained in cases where the patient is intelligent and co-operative.

Dosage.—The radium applicators used are all of full strength, i.e. 5 mg. per sq. cm. and are substantially unscreened—the contact surface consisting of 0·1 mm. monel metal. The most usual sizes are 1·0 and 1·25 cm. in diameter.

A typical applicator gives 6,000 r per hour on the surface and the intensity is uniform over the whole area of the applicator. The intensity falls off very rapidly in the surface layers of the cornea being about 50% at 1 mm. and 25% at 2 mm. This means that there is no considerable dosage to the lens, or indeed to the deeper layers of the cornea. This form of beta radiation is analogous biologically to hard gamma rays differing a good deal from soft X-rays in their effect. Treatment time is short and there is no caustic action, radiation reaction being slight or absent. The dosage, although it appears to be unusually high, is comparable with dosage by other forms of radiation allowing for the rapid fall-off in depth dose and for the fact that the biological efficiency is less.

Results.—42 cases of Mooren's ulcer have been seen at the Radium Institute since 1932. Two of these were not treated—in one case the first treatment was incomplete and the patient refused further treatment. In the other case the ulcer was exceedingly deep and conjunctivitis marked. This ulcer perforated a few days later and the eye was excised.

Of the 40 cases treated—21 occurred in men and 19 in women. The average age was 55. As a result of treatment 18 of these were healed and free from recurrence for periods of two years or more.

Thus: 1 for nine years, 1 for seven years, 1 for six years, 2 for five years, 10 for four years, 1 for three years, and 2 for two years.

11 other ulcers were known to be healed when last seen, but were lost sight of for varying periods of from four months to two years after treatment.

This would suggest that nearly half these cases did well, for periods long enough to hope that they would remain healed permanently and that over 25% of the rest did well primarily.

The picture is not quite so bright as this, for a high percentage of cases was bilateral on arrival—17 in all. A further 6 cases had primarily had ulceration in the other eye but this had been cured—in two cases by excision of the eye.

Of the 17 cases who had bilateral ulceration on arrival, 7 cases healed on both sides as a result of treatment, 4 cases healed on one side but not on the other, and the remaining 6 failed to heal on either side. Of the 6 cases in which one side had healed as a result of previous treatment, the more recently ulcerated cornea was healed in 3 cases.

brought me six different makes of lipstick that she used. Patch tests showed that two makes caused severe blistering, three others caused various degrees of redness and swelling and only one was free from reaction. Within a week of changing her lipstick to the innocuous variety her eye symptoms disappeared for ever.

The plants commonly causing trouble are primulas, chrysanthemums, dahlias, poison ivy and some virginia creepers. Usually there is some local irritation on the hands, but this may be so slight as to be scarcely noticed. Lids and conjunctiva are usually severely affected. Patch tests are necessary for the diagnosis of this type of sensitivity.

(2) The air-borne allergens are an important group and sensitivity to these allergens may be very difficult to deduce from the history. The common offenders are pollens, house dust (i.e. dust from disintegration of textiles, such as carpets, bedding, &c.), feathers, animal hairs and dandruff, orris root and moulds. Patting an animal and then rubbing the eyelids may cause a severe conjunctivitis in a sensitive person.

Since contact with house dust and feathers in bedding is very close and continuous it is difficult to obtain a direct history of irritation due to such contacts and routine testing by the intradermal method is required. Occasionally a clear-cut history is obtained, as for example a woman who had her first severe attack after spring cleaning and rubbing down wall paper and thereafter exacerbations whenever she used a brush and pan for cleaning the stair carpets. She did well on desensitization and changing to the use of a Hoover for cleaning purposes. In cases due to these allergens it is essential that the condition be explained to the patient and co-operation in avoidance of the irritating contacts obtained.

Where the actual irritating substance can be found and eliminated, results are excellent. Where it is found but cannot be wholly eliminated—partial elimination and desensitization give good results, the length of benefit being often proportional to the co-operation of the patient with regard to avoidance.

(3) Finally, a few cases of allergic eye reactions have been found due to ingestion of allergic food-stuffs. Children are most likely to be affected in this way. Wheat, milk and eggs are the most common allergens and I have seen cases due to all three. In my experience other allergic signs will be found somewhere in the body in all such cases.

ENDOGENOUS ALLERGY

Here we are on less sure ground and the results are equally uncertain. Focal eye reactions such as iritis may be due to bacterial allergy from sites of infections in teeth, tonsils, sinuses or even gall bladder. Here we can only treat by searching for and eliminating the focus, helping things in some cases by a bacterial vaccine. There is evidence of specificity of the vaccine in some cases, as the injections may cause a recrudescence of the iritis if an overdose is given. Cure following such treatment is not uncommon when the local focus can be easily dealt with. In bacterial allergy, skin tests are useless as almost all persons show skin reactions to the common bacteria. They have been abandoned by most allergists.

I have spoken almost entirely of the type of case where the pathologist can help. In other types of endogenous allergy particularly, little specific treatment is available. Benadryl and other anti-histamine drugs have a place, although a small one, in palliative treatment of certain cases.

Dr. J. T. Ingram: The term allergy covers those expressions of the individual which reflect his personal and peculiar sensitiveness to certain experiences and stimuli from within or without. I cannot see any great distinction between expressions which arise from vague, general or indifferent causes and those which arise from definite and recognized stimuli. We must not, because of the magic word allergy, feel that a dermatitis of the lids provoked by eye-shadow is to be placed in a different field from a dermatitis produced by rubbing and scratching and consequent upon a psychogenic pruritus.

In the former case we have recognized one material factor to which the tissues are sensitive and the exhibition of that material will always revive the tendency to reaction—it has become a habit, like a conditioned reflex. In the latter case—the neurodermatitis—the stimulus is not a specific or a recognized material one though, no doubt, some material metabolite produced by nervous, endocrine or other activity is as definitely responsible as the exogenic agent in the cosmetic. In this latter case too the factor of habit-formation is by no means absent. We must remember that not only individuals but their several and particular tissues are as habit forming as the famous horse of Evesham.

I would, therefore, start from the individual, giving consideration to all those influences, endogenic and environmental, which bear upon his physiological tone and pathological reactions.

Allergic reaction.—It would seem probable that the allergic reaction is merely incidental and not related to immunity, that it serves no very useful purpose and is only harmful

[*March* 13, 1947]

DISCUSSION ON ALLERGY IN OPHTHALMOLOGY

Mr. Gayer Morgan in his opening remarks gave a short description of what was meant by allergy and the allergic reaction. He stressed its great importance in clinical medicine and pointed out that almost every disease of the eye had been reported as allergic in origin in some particular case. It was necessary to find some underlying feature which would suggest allergy, and so he discussed the type of person who is naturally allergic by inheritance, and those people who develop the tendency during the normal periodic stresses and strains of life, or the abnormal worries and frustrations which are such frequent accompaniments of modern existence. These produce a mental and physical exhaustion and so predispose to hypersensitivity. In this state there are biochemical changes, endocrine disturbances and liver dysfunction, and a person becomes sensitive to many different antigens, the one to which he falls depending on his environment.

Characteristics of the allergic reaction were discussed. The patient's complaints are far in excess of the actual condition found—waxing and waning of the symptoms is a prominent feature. Tissue fluid mobilization is very characteristic, and on these lines many different pathological conditions were considered affecting the lids, conjunctiva, cornea, iris and ciliary body, lens, choroid and retina.

The question of migraine and epilepsy as possibly allergic phenomena was discussed.

Dr. C. J. C. Britton: *Allergy in ophthalmology from the point of view of a clinical pathologist.*—Before an allergic investigation is undertaken it is essential that a local bacterial infection in the eye shall be excluded. It is surprising in how many chronic, mild or moderately severe cases the cause of the chronicity is a bacterial infection, even although the fundamental basis may be a true allergic sensitization to an exogenous allergen such as house dust, &c. Of course some cases are wholly bacterial and I have seen a number of cases in which *Staph. aureus, H. influenzæ* and even β hæmolytic streptococci have been the cause of a longstanding but relatively, in fact surprisingly, mild conjunctivitis.

Once infection has been excluded a presumptive indication of an allergic ætiology in a conjunctivitis may be determined by examining a smear of the discharge from the eye for eosinophils. In actual fact this examination is often omitted, as although the presence of numerous eosinophils is of importance in a positive way, occasionally eosinophils may be absent in some cases in which there is no doubt as to the allergic basis. Thus, I have sometimes failed to find eosinophils even in cases of true pollen conjunctivitis.

The next stage is to take the full history as to asthma, hay fever, skin troubles, urticaria, stuffy noses, sneezing attacks or severe chronic catarrh, migraine and bilious attacks. A positive family history is suggestive.

Next comes the history of the onset, the periodicity and the time of day when worst, and the use of drugs.

Based on these replies skin tests are carried out—intradermal, scratch or patch tests.

Allergic eye conditions may be due to three main causes: drugs used locally; endogenous allergens; exogenous allergens.

Drugs used locally.—Some of the less rare offenders in this group are atropine, yellow oxide of mercury, zinc sulphate, cocaine and allied anæsthetics, penicillin and sulphonamides.

The endogenous allergens include the cases due to bacterial or bacterial toxin allergy and cases due possibly to metabolic or endocrine disturbances. These cases are most difficult to diagnose, in fact the diagnosis is largely by exclusion.

EXOGENOUS ALLERGY

The exogenous allergens form an extremely wide group and may be subdivided into:—

(1) Contact irritants other than drugs; (2) airborne irritants; (3) ingestants.

Contact irritants other than local drugs.—The common offenders in this group are cosmetics, certain plants, and occupational dusts and contactants. Common cosmetics causing trouble are hair dyes (aniline or vegetable), shampoos, face powders, wave-setting lotion, lipstick and nail polish or polish remover. I have seen cases with lesions entirely or almost entirely confined to the eyes due to all of these. It is curious how little irritating effect say nail polish or shampoo may have on the fingers or scalp and yet the conjunctivitis may be severe and swelling of lids marked. In one case, that of a lady who had had severe irritation of the conjunctiva and swelling of the lids for many months despite all types of local treatment, the irritation at night was so severe as to make her almost suicidal. Testing for sensitivity to all the usual allergens proved negative until the patient stated in general conversation that her lips tended to get rather dry. Clinically there was no obvious lesion on the lips. She brought me six different makes of lipstick that she used. Patch tests showed that two makes caused severe blistering, three others caused various degrees of redness and swelling and only one was free from reaction. Within a week of changing her lipstick to the innocuous variety her eye symptoms disappeared for ever.

The plants commonly causing trouble are primulas, chrysanthemums, dahlias, poison ivy and some virginia creepers. Usually there is some local irritation on the hands, but this may be so slight as to be scarcely noticed. Lids and conjunctiva are usually severely affected. Patch tests are necessary for the diagnosis of this type of sensitivity.

(2) The air-borne allergens are an important group and sensitivity to these allergens may be very difficult to deduce from the history. The common offenders are pollens, house dust (i.e. dust from disintegration of textiles, such as carpets, bedding, &c.), feathers, animal hairs and dandruff, orris root and moulds. Patting an animal and then rubbing the eyelids may cause a severe conjunctivitis in a sensitive person.

Since contact with house dust and feathers in bedding is very close and continuous it is difficult to obtain a direct history of irritation due to such contacts and routine testing by the intradermal method is required. Occasionally a clear-cut history is obtained, as for example a woman who had her first severe attack after spring cleaning and rubbing down wall paper and thereafter exacerbations whenever she used a brush and pan for cleaning the stair carpets. She did well on desensitization and changing to the use of a Hoover for cleaning purposes. In cases due to these allergens it is essential that the condition be explained to the patient and co-operation in avoidance of the irritating contacts obtained.

Where the actual irritating substance can be found and eliminated, results are excellent. Where it is found but cannot be wholly eliminated—partial elimination and desensitization give good results, the length of benefit being often proportional to the co-operation of the patient with regard to avoidance.

(3) Finally, a few cases of allergic eye reactions have been found due to ingestion of allergic food-stuffs. Children are most likely to be affected in this way. Wheat, milk and eggs are the most common allergens and I have seen cases due to all three. In my experience other allergic signs will be found somewhere in the body in all such cases.

ENDOGENOUS ALLERGY

Here we are on less sure ground and the results are equally uncertain. Focal eye reactions such as iritis may be due to bacterial allergy from sites of infections in teeth, tonsils, sinuses or even gall bladder. Here we can only treat by searching for and eliminating the focus, helping things in some cases by a bacterial vaccine. There is evidence of specificity of the vaccine in some cases, as the injections may cause a recrudescence of the iritis if an overdose is given. Cure following such treatment is not uncommon when the local focus can be easily dealt with. In bacterial allergy, skin tests are useless as almost all persons show skin reactions to the common bacteria. They have been abandoned by most allergists.

I have spoken almost entirely of the type of case where the pathologist can help. In other types of endogenous allergy particularly, little specific treatment is available. Benadryl and other anti-histamine drugs have a place, although a small one, in palliative treatment of certain cases.

Dr. J. T. Ingram: The term allergy covers those expressions of the individual which reflect his personal and peculiar sensitiveness to certain experiences and stimuli from within or without. I cannot see any great distinction between expressions which arise from vague, general or indifferent causes and those which arise from definite and recognized stimuli. We must not, because of the magic word allergy, feel that a dermatitis of the lids provoked by eye-shadow is to be placed in a different field from a dermatitis produced by rubbing and scratching and consequent upon a psychogenic pruritus.

In the former case we have recognized one material factor to which the tissues are sensitive and the exhibition of that material will always revive the tendency to reaction—it has become a habit, like a conditioned reflex. In the latter case—the neurodermatitis—the stimulus is not a specific or a recognized material one though, no doubt, some material metabolite produced by nervous, endocrine or other activity is as definitely responsible as the exogenic agent in the cosmetic. In this latter case too the factor of habit-formation is by no means absent. We must remember that not only individuals but their several and particular tissues are as habit forming as the famous horse of Evesham.

I would, therefore, start from the individual, giving consideration to all those influences, endogenic and environmental, which bear upon his physiological tone and pathological reactions.

Allergic reaction.—It would seem probable that the allergic reaction is merely incidental and not related to immunity, that it serves no very useful purpose and is only harmful

[*March* 13, 1947]

DISCUSSION ON ALLERGY IN OPHTHALMOLOGY

Mr. Gayer Morgan in his opening remarks gave a short description of what was meant by allergy and the allergic reaction. He stressed its great importance in clinical medicine and pointed out that almost every disease of the eye had been reported as allergic in origin in some particular case. It was necessary to find some underlying feature which would suggest allergy, and so he discussed the type of person who is naturally allergic by inheritance, and those people who develop the tendency during the normal periodic stresses and strains of life, or the abnormal worries and frustrations which are such frequent accompaniments of modern existence. These produce a mental and physical exhaustion and so predispose to hypersensitivity. In this state there are biochemical changes, endocrine disturbances and liver dysfunction, and a person becomes sensitive to many different antigens, the one to which he falls depending on his environment.

Characteristics of the allergic reaction were discussed. The patient's complaints are far in excess of the actual condition found—waxing and waning of the symptoms is a prominent feature. Tissue fluid mobilization is very characteristic, and on these lines many different pathological conditions were considered affecting the lids, conjunctiva, cornea, iris and ciliary body, lens, choroid and retina.

The question of migraine and epilepsy as possibly allergic phenomena was discussed.

Dr. C. J. C. Britton: *Allergy in ophthalmology from the point of view of a clinical pathologist.*—Before an allergic investigation is undertaken it is essential that a local bacterial infection in the eye shall be excluded. It is surprising in how many chronic, mild or moderately severe cases the cause of the chronicity is a bacterial infection, even although the fundamental basis may be a true allergic sensitization to an exogenous allergen such as house dust, &c. Of course some cases are wholly bacterial and I have seen a number of cases in which *Staph. aureus*, *H. influenzæ* and even β hæmolytic streptococci have been the cause of a longstanding but relatively, in fact surprisingly, mild conjunctivitis.

Once infection has been excluded a presumptive indication of an allergic ætiology in a conjunctivitis may be determined by examining a smear of the discharge from the eye for eosinophils. In actual fact this examination is often omitted, as although the presence of numerous eosinophils is of importance in a positive way, occasionally eosinophils may be absent in some cases in which there is no doubt as to the allergic basis. Thus, I have sometimes failed to find eosinophils even in cases of true pollen conjunctivitis.

The next stage is to take the full history as to asthma, hay fever, skin troubles, urticaria, stuffy noses, sneezing attacks or severe chronic catarrh, migraine and bilious attacks. A positive family history is suggestive.

Next comes the history of the onset, the periodicity and the time of day when worst, and the use of drugs.

Based on these replies skin tests are carried out—intradermal, scratch or patch tests.

Allergic eye conditions may be due to three main causes: drugs used locally; endogenous allergens; exogenous allergens.

Drugs used locally.—Some of the less rare offenders in this group are atropine, yellow oxide of mercury, zinc sulphate, cocaine and allied anæsthetics, penicillin and sulphonamides.

The endogenous allergens include the cases due to bacterial or bacterial toxin allergy and cases due possibly to metabolic or endocrine disturbances. These cases are most difficult to diagnose, in fact the diagnosis is largely by exclusion.

EXOGENOUS ALLERGY

The exogenous allergens form an extremely wide group and may be subdivided into:—

(1) Contact irritants other than drugs; (2) airborne irritants; (3) ingestants.

Contact irritants other than local drugs.—The common offenders in this group are cosmetics, certain plants, and occupational dusts and contactants. Common cosmetics causing trouble are hair dyes (aniline or vegetable), shampoos, face powders, wave-setting lotion, lipstick and nail polish or polish remover. I have seen cases with lesions entirely or almost entirely confined to the eyes due to all of these. It is curious how little irritating effect say nail polish or shampoo may have on the fingers or scalp and yet the conjunctivitis may be severe and swelling of lids marked. In one case, that of a lady who had had severe irritation of the conjunctiva and swelling of the lids for many months despite all types of local treatment, the irritation at night was so severe as to make her almost suicidal. Testing for sensitivity to all the usual allergens proved negative until the patient stated in general conversation that her lips tended to get rather dry. Clinically there was no obvious lesion on the lips. She enlightening, but I will first consider certain granulomata provoked by drugs, toxins and infective organisms. The conjunctiva, as well as the skin, may participate in such reactions.

Granulomatous reactions occur on the lids from sensitiveness to drugs like bromides and iodides, the former being more common in infants.

But in this group we naturally turn to those reactions associated with infective organisms as the treponema of syphilis and the tubercle bacillus.

In tuberculosis, I have seen erythema nodosum—the earliest of the sensitization reactions—on the face and presume it may attack the lids. The Mantoux reaction is strongly positive. I believe that phlyctenular conjunctivitis may be of this character but in my department at Leeds which deals with about 6,000 new cases a year and several hundred cases of tuberculous skin disease, phlyctenular conjunctivitis is hardly ever seen.

The papulo-necrotic tuberculide—the superficial gummatous tuberculide—is the reaction more commonly seen and is related to a later stage of the disease. So far as the skin itself is concerned the affection is not a serious one and is rarely associated with any severe degree of infection of viscera or glands, but in the eye it can, presumably, cause much disorganization. There is a strong positive reaction to the Mantoux test. Though dependent for its character upon the age of the infection, it would seem that only certain types of individual are susceptible. We know little of the type except that there would seem to be some disturbance of endocrine balance exercising an effect on neurovascular tone and these subjects are peculiarly susceptible to climatic influences.

In the absence of any major tuberculous disease demanding attention, the best treatment is to seek a suitable climate, though empirical remedies such as arsenic, gold and tuberculin injections are of some value.

Lupus vulgaris is another peculiar and personal type of reaction to the tubercle bacillus, and may occur on lids and conjunctiva.

Sarcoidosis may be tuberculous, shows a negative or minimal reaction to the Mantoux test, is uncommon on the lids but may occur. Uveoparotitis I believe to be tuberculous but do not include in sarcoidosis.

There is a group of eruptions we call tuberculides and which particularly affect the face, including the lids—acnitis, acne agminata, follicular lupus of Tilbury Fox and the rosaceous tuberculide of Lewandowsky. On rare occasions these may be sensitization reactions to tuberculous disease, but in the majority of cases there is no evidence to support the suggestion.

Rosacea.—The lids are commonly involved and lesions occurring on the conjunctiva may give rise to serious ulceration and scarring. Rosacea is an affection of rather acute character producing a chronic pattern of allergic reaction. It is not dependent upon any single stimulus—infective or otherwise—but is intimately bound up with the individual pattern of patient, has great psychological significance, is influenced to a marked degree by endocrine function and vasomotor tone and is variably linked with a number of nutritional and other factors. At the same time response to local treatment is often dramatic.

Finally, any conception of allergy is unfortunate that confines our views upon a subject which in fact covers the greater part of the field of medicine and pathology. Conceptions and practices based upon ideas of skin tests or a few particular biochemical reactions and methods of desensitization must limit our vision. Treatment is still in large part empirical. Work on the anti-histamine preparations may give us another useful weapon.

Mr. Eugene Wolff mentioned a lady aged about 50 who had a painful eye, with tension, every time she got an attack of urticaria. The condition was promptly cured when 0·5 c.c. of adrenaline was injected subcutaneously.

Dr. Eric Lipman Cohen said that Dr. Britton had overrated the value of the intradermal test. A negative intradermal test meant nothing, and a positive intradermal test did not mean that the cause of the patient's symptoms had been found. It had been shown repeatedly that nearly all infants would give a positive intradermal test to certain substances, notably eggs, but these children would not necessarily get symptoms from ingesting eggs. Again, to recommend intradermal testing to those who were not doing it all day long was a dangerous thing, because patients had been known to collapse during these tests. Although scratch tests were less satisfactory technically, they were much safer.

With regard to benadryl causing drowsiness in the daytime, that could be arrested by giving in the morning a small dose of amphetamine sulphate.

Dr. E. Felix said that the whole science of allergy was nothing else but the science of symptoms. Nothing indicative of irreversible allergic tissue changes are found post mortem, when it involves a vital organ or tissue. The practical value and significance of skin tests—scratch and intradermal—are limited and they have added not a little to our confusion.

In the biochemical field little has yet been achieved but research is obviously necessary and important. The problem is complicated by the secondary biochemical disturbances set up by the production of histamine in the allergic reactions themselves. The researches of Lewis have shown much of the nature of the acute physiological reactions consequent upon the action of histamine-like substances upon blood-vessels.

The pathological reactions, transient and persistent, are various and show a focal œdema and degeneration of connective tissue which may proceed by histiocytic proliferation to granulomata of the rheumatic or tuberculoid patterns or to eosinophilic infiltrations. These are being clearly defined and correlated.

Clinical features—acute.—On the clinical side we have to distinguish between reactions which are primarily epidermal and those which are dermal. Reactions sometimes relate to particular tissues, as to lens tissues in cataract or to vessel walls in polyarteritis nodosa.

We must differentiate between acute reactions, almost physiological in character, and those of a more chronic and pathological character as from some drugs, toxins and organisms.

Epidermal and some dermal reactions are acute and tend to be of a catarrhal type like eczema or dermatitis, or urticaria. The eyes and eyelids figure conspicuously in the emotional life of the human animal. The eyelids are a favourite site for itching and neurodermatitis of emotional origin. Œdema is readily evoked by rubbing and may be confused with urticaria or with the swelling of a contact dermatitis.

Contact dermatitis—dependent upon specific sensitiveness to some material making contact with the skin—arises from cosmetics, including face creams and powders and those used on the eyebrows, lids, lashes and in the eyes. Nail varnish, without causing dermatitis on the fingers, may provoke a dermatitis of the lids or face by contact. Swelling of the scalp from dermatitis due to hair-dyes may present itself as œdema of the lids. The eyelids are sometimes involved in dermatitis due to spectacle frames, but the ears are the site of election. Actinic rays, vapours, dusts, pollens and plant emanations may be an exciting cause, but in this age of therapeutic danger we must remember local applications to the lids or conjunctiva. Penicillin and sulphonamides head the list at the moment, but atropine, mercurial applications and boracic acid are always with us, giving rise to what the dermatologists called "spectacle dermatitis" before they were confronted with the hazards of the plastic spectacle frames.

These cases in which the conjunctiva as well as the skin may be affected are in the nature of detective problems, and the diagnosis can be confirmed in the majority by the application of a patch-test of the agent under suspicion to the upper arm. Sensitization of this specific character, when once established, generally persists for many years or for life, though in some instances it is related to a temporary disturbance of health or tone and may clear when that is corrected. Attempts at desensitization are not, I think, often successful or justifiable if the agent can be avoided.

Treatment of the reaction is by simple alkaline lotions locally and alkalies internally.

The group of seborrhœic ills must be considered in relation to differential diagnosis, as must erysipelas and infection of underlying tissues.

Urticaria may be localized to the lids and conjunctiva as in angioneurotic œdema and may, like dermatitis, be due to non-specific influences, emotional causes or may arise from specific sensitization to penetrating contacts or to blood-borne stimuli as foodstuffs, drugs, metabolic or infective toxins. The problem calls for the most careful physical overhaul and an assessment of the patient as an individual and his relationship to his environment, in its widest sense.

Among causative drugs the aspirin group is worthy of special mention.

Bullous eruptions and purpura are of somewhat related significance and call for similar considerations.

These epidermal and urticarial reactions are of a transient, evanescent character—they may be regarded as the acute sensitization reaction in which the stimulus, whether it be emotional or material, acts upon the physiological balance of the individual for a short period. The characteristics of the lesion are determined by an upheaval in vascular function related to blushing. The reaction is an expression of disapproval and will pass when equanimity is restored.

Clinical features—chronic.—The more chronic ills relate less to function than to structure; they are essentially pathological in character. The individual rather than the stimulus is still the central feature of the problem but he is now diseased and not merely disturbed. The characters of the lesion turn upon the behaviour of the fixed tissue cells and not upon vascular tone. There are a number of intermediate states, as rosacea, which are very

Section of Psychiatry

President—Professor AUBREY LEWIS, M.D.

[March 11, 1947]

Disorders of Skill: An Experimental Approach to Some Problems of Neurosis. [*Abstract*]

By D. RUSSELL DAVIS, M.D., M.R.C.P., D.P.M.

Medical Research Council, Applied Psychology Research Unit, Cambridge

SKILL connotes adaptation to the environment, and the hypotheses which are developed to explain disorders of skill may also explain the disorders of adaptation which constitute neurosis. There are precedents in research on experimental neurosis for the explanation of clinical problems by hypotheses derived from the laboratory study of disordered behaviour. The study of disorders of skill, however, has certain advantages over that of experimental neurosis, namely: human subjects are employed, and observations of variations in behaviour are amplified by reports of associated variations in feeling; slight variations of stimulus conditions may cause disturbances of activity, which, because they do not amount to complete breakdown, can readily be recorded and scored with the same devices as the normal behaviour; hence the nature of the disturbances can be defined clearly. It was possible, in the case of the disorders studied by the author, to show that the type and degree of the disorder in different individuals were dependent upon the kind and degree of neurotic predisposition (Davis, 1946*a*).

Following the lead of Pavlov, many experimenters have tried to relate experimental disorders to processes in the central nervous system, and their theories deal with the mechanism of disorder. To show how stimuli become connected with responses and with each other, the laws of association have been invoked, such as the Law of Exercise. A more interesting problem, however, is the nature of the external situation in which a given disorder arises. Not only actions have then to be considered, but the effects of actions, and reference has to be made to the Law of Effect. Whenever a principle stating how effects determine behaviour has been applied to the explanation of neurosis, however, the difficulty has inevitably been encountered that in neurosis behaviour persists, whose effects appear to be more punishing than rewarding; whereas, if the second half of the Law of Effect is valid, the tendency to a mode of behaviour, accompanied, or closely followed by punishment, should be weakened. Freud resolved the difficulty by supposing that, although apparently punishing, neurotic activity is adaptive from the standpoint of the inner needs of the individual. Other attempts at resolution have involved reversion to laws of association (e.g. Freud's principle of repetition—compulsion). Mowrer and Ullman (1945) have recently put forward an attractive theory. An alternative theory was suggested by the author's researches.

Explanation was sought of the excessive activity observed in experiments with the Cambridge Cockpit (Davis, 1946). Although it was accompanied by a progressive increase in anxiety, this activity persisted in apparent contradiction to the second half of the Law of Effect. First it was supposed that the subjects of the experiments were motivated by *anticipatory tension*, relating to the danger of failure to attain a satisfying standard of performance. Anticipatory tension is a secondary drive which has been postulated to account for the results of the experiments called "instrumental avoidance training" by Hilgard and Marquis (1940). Tension might be reduced, if a subject gained effective control of the machine, but, since the conditions of the tests nothing conclusive that allergy is the only causative factor even in periarteritis nodosa. He thought they should tackle the allergy problem without looking upon allergy as a disease. Advance might be made if they took into account the feature of faulty intracellular metabolism, especially the breakdown of proteins and carbohydrates, which in the first instance permits an individual to become allergic.

Dr. Vera Walker said that in 1941 it was decided to hold an Allergy Clinic at the Oxford Eye Hospital once a week, although it was doubtful whether a sufficient number of allergic cases would present themselves to justify such a clinic. An endeavour was to be made to find out whether there could be any allergic cause underlying the many chronic cases which attend this and other Eye Hospitals year after year, and which have in the past appeared to derive no benefit from any routine treatment. About 17,000 cases pass through the general Out-patient Department of the Oxford Eye Hospital each year, and taking the average from 1941 until the present time 2% (340 cases) of all these patients had been satisfactorily proved to be allergic, not only by skin tests, but also by removing the offending allergens and then trying to reproduce the symptoms by further contact. Among these 340 cases, 55% suffered from conjunctivitis, 2·9% from keratitis, 3% from iritis and iridocyclitis, 0·1% from cataract and 36% from migraine.

Out of 47 cases of iritis investigated during the year ended September 1946, six were allergic and belonged to allergic families, eight were rheumatic and three of psychological origin. The remaining thirty cases were still awaiting diagnosis. Of the six allergic cases, three had iritis associated with asthma at some stage in their lives; two had iritis in the summer only, and were found to be allergic to a specific pollen. The sixth case was that of a farmer's wife, aged 57, who had had recurrent iritis and iridocyclitis during twenty years. Between 1942 and 1945 she was in hospital seven times for treatment. There was a family history of asthma and of osteoarthritis. Allergy tests showed a high sensitiveness to house dusts, to orris and to cats, and it was discovered that for twenty years, when she was not in hospital, she had slept with a cat on her pillow. Since desensitization she has remained well for eighteen months.

Dr. D. Harley said that none of the speakers had thought fit to say what they meant by allergy. It was not possible to speak of "allergy" in a definitive way any more than of "indigestion". Allergy was not one specific disease or condition but a group of conditions. He suggested that some of the apparent confusion and conflict of opinions during the meeting was due to some of the speakers not understanding clearly what the other man meant by "allergy". Some attempt must be made to define what was meant by allergy and to give some description of the various groups of allergic phenomena.

Mr. Gayer Morgan, in reply, said that the question of allergy needed the full co-operation of the physician, biochemist and pathologist, and until they could tell us exactly what were the true characteristics of the allergic reaction and the correct place it took in clinical medicine, and why an individual could acquire the tendency to pervert what was, after all, part of the protective mechanism of the body so that it became a disease, we must remain very much in the dark as regards diagnosis and treatment.

Dr. C. J. C. Britton said that, in the use of vaccines, the difference between the immunization dose and the dose in desensitization was difficult to decide. It was a personal question in every case. Usually the dose of a vaccine for desensitization was at least one-tenth of the strength used for immunization. For desensitization a minute dose was used and built up, and no more than a mild reaction must ever be obtained. If such a reaction did occur a lower dose must be given and gradually increased.

With regard to clinical diagnosis of allergic ophthalmic disease he could not determine on appearance alone which cases were true allergies. The intradermal or scratch test might be extremely useful, but the patient as a whole must be dealt with.

Dr. J. T. Ingram, also in reply, said that allergy was not a matter of symptoms only; the point he had tried to bring out was that there were physiological and pathological patterns in allergy. He did not think he could have given a simple definition of allergy.

The following case was shown:

Penicillin and Sulphonamides as a means of Arresting Cavernous Sinus Thrombosis in a Case of Pneumonia complicated with Ophthalmic Symptoms.—R. LINDSAY-REA, F.R.C.S.

[*April* 8, 1947]

DISCUSSION ON THE SOCIAL ASPECTS OF HOMOSEXUALITY

[*Summary*]

Dr. E. A. Bennet: The purpose of this paper is to discuss the social distinctness of the adult homosexual and some of the reasons for it; and to point out our ignorance of certain aspects of male and female homosexuality and the advantages which might be expected to follow increased knowledge. The interests and aspirations of our society in family life promote a solidarity in which the homosexual has little or no part. The feeling of difference, the social stigma, the legal penalties—all these close off the domain of inversion. Although an indictment cannot be preferred against a woman for a homosexual act, lesbianism receives no official or articulate social sanction.

I.—The disapproval extended to inverts is in part explained by the abhorrence felt for the discreditable acts, happily rare, which are publicized in the newspapers when legal action is taken against a homosexual. Such accounts provide for many their only information about homosexuality and they conclude that all homosexuals are reprehensible. Amongst homosexuals, as amongst normal people, every variety of character is found. The attitude of homosexuals themselves towards inversion varies and some bitterly regret their exclusion from family life. The doctor and the lawyer tend to see unstable homosexuals; and it is therefore unwise for them to generalize. But I doubt if social instability is commoner among homosexuals as a whole than amongst heterosexuals.

Nevertheless, the social status of homosexuality in this country implies that the invert is a danger to society. The seducer of boys and girls be he homosexual or heterosexual is clearly a social menace. The number of persons found guilty of such crimes forms a small percentage of the homosexual population, and homosexuality among adult males has been condemned for other reasons. The average man may feel justified in condemning it as abnormal, unnatural and unproductive; and also he considers that if he did not condemn it, or scoff at it, it might be thought that he approved of it. Silverberg [1], a psychoanalyst, claims that passive male homosexuality is condemned because its ultimate strategic aim is to extinguish the race. The opinion of the man-in-the-street to-day in this country on homosexuality is emotionally tinged, subjective and largely determined by hostile prejudice.

A danger with which a homosexual is faced is blackmail. This is perhaps one of the chief reasons why the homosexual is silent. It will hardly be disputed that our knowledge of homosexuality as a social phenomenon is fragmentary and that we are in no position to adopt an attitude of complacency or of wholesale condemnation.

II.—Psychiatry to-day is overnourished with theory and undernourished by facts—facts acquired and tested by observation. We are liable to project unwittingly and to propound theories of homosexuality without substantial knowledge of the social phenomenon itself. We do not know the number of homosexuals in this country. Havelock Ellis [2] gave it as his opinion: "That we may probably conclude that the proportion of inverts is slightly over 2%. That would give the homosexual population of Great Britain as somewhere over a million." Myerson and Neustadt [3], declare that statistics vary from "as high as more than 50% of an unselected population to as low as 2%". Davis [4], writing of homosexuality among unmarried college women, states that 26% of a group of 1,200 women college graduates have had intense emotional relationships accompanied by overt physical practices with other women. Conditions in Great Britain are different from those in America and it would be rash to draw conclusions from these figures about the incidence of homosexuality in this country where no systematic sociological inquiry has been made.

did not favour success, tension tended to increase. Secondly it was supposed that an increase in anticipatory tension is reflected in an increase in the amount and vigour of activity. This increase in activity would generally be of biological value in emergency, as Cannon (1929) argued in the similar case of emotion, but it occurs even though its effects are disastrous, and it is not lessened by punishment. Increase in the amount and vigour of activity impaired performance in the experiments, because of the constraints of the situation, and especially because of the design of the apparatus. Attainment declining, and the danger of failure becoming more imminent, anticipatory tension increased more, and the consequent increase in activity caused a further decline in attainment. Thus a vicious circle was set up, which was stopped only by the development of a new form of disorder which was called the "withdrawal reaction".

The competence of this theory to explain the overactive form of disorder in the cockpit experiments was proved by devising a new situation, the "Skilled Response" test, in which according to the theory similar effects would be expected to occur, and by demonstrating that these effects did, in fact, occur. Thus under conditions (ambiguous stimuli) in which it could be assumed that anticipatory tension was increased, skilled responses were more extensive, more precipitate, more disturbed by restless movements and less accurate than under conditions (simple stimuli) in which anticipatory tension was normal. No success has yet been achieved in devising a similar proof of a hypothesis explaining the "withdrawal" form of disorder. The features of this disorder (retarded responses of small range) were also shown in the performance on the "Skilled Response" test of those of a miscellaneous group of neurotic patients who were diagnosed as hysterical.

Application of the theory to neurosis leads to the following conclusions. Neurosis is quite distinct from health, and it is wrong to say that all individuals are more or less neurotic, or that clinical disorders are at the extreme of a distribution which includes the healthy. Neurosis begins at a point at which in a given situation an increase in anticipatory tension impairs adaptation, and at which the vicious circle of increasing tension—decreasing attainment is instituted. Anticipatory tension (or anxiety, to which it is equivalent) may increase without the development of neurosis, if it does not impair powers of adaptation. The more restrained are the responses which a situation requires, the more readily does an increase in anticipatory tension lead to impairment of powers of adaptation. It is not necessary to suppose that the disasters which befall the anxious are motivated by masochistic or any other gratification, since, if it leads to impairment of performance, tension may make inevitable the very disaster of which it is anticipatory, or, by leading to an impulsive action, create a situation to which adaptation is impossible. If anticipatory tension increases to a point at which powers of adaptation are impaired, the consequences cannot be prevented by an effort on the part of the sufferer.

In the cockpit experiments, various types of interference by the experimenter were shown to cut short the overactive form of disorder, but the "withdrawal" form was not readily influenced. The problem of the persistence of activity in these experiments is analogous to that of the origin of neurosis. Further research is necessary to explain the "withdrawal" form of disorder and, hence, to elucidate the psychopathology of fully developed neurosis.

REFERENCES

CANNON, W. B. (1929) Bodily Changes in Pain, Hunger, Fear and Rage. Second Edition. London.
DAVIS, D. R. (1946) *J. Neurol. Neurosurg. Psychiat.*, 9, 23.
—— (1946*a*) *J. Neurol. Neurosurg. Psychiat.*, 9, 119.
HILGARD, E. R., and MARQUIS, D. G. (1940) Conditioning and Learning. N. York.
MOWRER, O. H., and ULLMAN, A. D. (1945) *Psychol. Rev.*, 52, 61.

The full paper will be published in the *Quarterly Journal of Experimental Psychology*.

women admit overt homosexual activities—and the same is probably true of men—the severity of public disapprobation comes to be understood as arising, to some degree, from a sense of guilt on the part of the heterosexual majority and not entirely from the supposed depraved quality of inversion. In the study of sexual deviation our chief need to-day is for facts on which to base our medical, educational, legal and ethical conceptions of the social aspects of homosexuality.

REFERENCES

1 SILVERBERG, W. V. (1938) *Psychiatry*, 1, 51.
2 ELLIS, HAVELOCK (1915) Sexual Inversion. 3rd Edition. London. 64.
3 MYERSON, A., and NEUSTADT, R. (1942) *Clinics*, Philadelphia, 1, (4), 945.
4 DAVIS, KATHARINE BEMENT (1929) Factors in the Sex Life of Twenty-two hundred Women, New York. 277.
5 FENICHEL, OTTO (1945) The Psycho-Analytic Theory of Neuroses, London. 112.
6 ALLEN, CLIFFORD (1940) The Sexual Perversions and Abnormalities, London, 182.
7 ANOMALY (1929) The Invert, London, 16.
8 CURRAN, D. (1938 and 1947) *Practitioner*, 141, 287, and 158, 348.
9 ELLIS, HAVELOCK (1915) op. cit. 59.
10 FREUD, S. (1924) *Collected Papers II*, 211, 207.
11 STOLLER, ALAN (1946) *The Medical Press*, 216, 266.

Dr. H. Mannheim: Criminology—in its widest sense as including Penology—has four main functions:

(1) To define the conception of crime (the purely legal definition is tautological and therefore useless for our purposes) and to fix the boundaries of the criminal law, i.e. to determine the types of human behaviour which should be punished.

(2) To collect and analyse the facts about crime and the criminal; to study the causes and the whole structure of crime in individual countries and localities; and, finally, to integrate and, as far as possible, to reconcile the different views and methods of the psychologist and psychiatrist, the anthropologist and biologist, the sociologist and the lawyer, by providing a centre, a neutral territory where they all can meet on equal terms.

(3) To study the penal systems, past and present, and the effect of the various methods of dealing with lawbreakers and of crime prevention as applied in different countries.

(4) To prepare the ground for legislative and administrative reform, especially through teaching and educating public opinion.

If the problem of homosexuality is approached on such lines, the following points will have to be made:

(*a*) Should homosexual activities be punished as crimes? It is one of the fundamental lessons which Criminology has to teach that only such forms of human behaviour should be punishable which are distinctly anti-social, i.e. harmful to the community at large; which arouse a strong communal feeling of indignation so as to make sure the support of the public in enforcing the law; which can be defined in legal terms and are of such a character as to make the production of evidence in a criminal court not an impossible task.

In England, homosexuality remained a purely ecclesiastical crime until 1533. This ecclesiastical origin of the penal law on the subject should make us particularly cautious as it may explain much of the moral indignation and of the resulting social stigma. It would also seem to justify the demand for an unbiased scientific investigation into the nature, strength, and origin of that feeling of moral indignation, to find out, e.g., how far it is related to homosexual activity itself and how far it may be only the result of the harsh treatment meted out to behaviour of this kind by the law. Degrading penalties have attached a social stigma to human behaviour that would otherwise not have been regarded as infamous. Granted that homosexual love between women differs in many ways from that between men, it would be an interesting

We need, and need badly, a fact-finding investigation. The social problem of homosexuality is of such importance that a representative committee, with wide terms of reference, should be formed to accumulate information. Facts are needed regarding the number of homosexuals, the significance of constitutional and hereditary factors, the effects of environmental influence in schools and elsewhere, the results of psychiatric treatment, and the consequences of punitive measures upon homosexual and bisexual persons of both sexes. An alteration of the Law as it affects those found guilty of homosexual offences would be more likely to succeed if backed up by an array of facts.

The members of the proposed fact-finding committee would have to decide what questions needed answers. Take Education for example. We are uncomfortably aware of our ignorance regarding the effect of homosexual proclivities or acts amongst adolescents. Are these modified or increased by co-education and the public school system? Fenichel [5] considers that: "Occasional homosexual experiences between adolescents should not be looked upon as pathological so long as they appear as temporary phenomena of adaptation and do not result in definite fixations." The results of such experiences, or experiences with older youths or adults (both of which I regard as morbid), upon normally constituted adolescents are certainly not uniformly disastrous. But when the adolescent is of imperfect constitution, the results may be severe.

Doctors who are free to look at the problem of homosexuality objectively would welcome a fact-finding inquiry into the results of psychiatric treatment—a matter on which there is conflict of opinion. Allen [6] has reported on two patients both of whom recovered completely; and he points out that many cures are recorded in the literature. Ernest Jones [7] claims that psychoanalysts are able to obtain a large proportion of cures amongst inverts. I have personal knowledge of men whose sexual instincts are now normally directed who for long regarded themselves as homosexual. Curran [8], on the other hand, doubts the efficacy of psychotherapy with inverts.

There is no accepted criterion of homosexuality of which there are many forms and degrees; and the term itself is used in varying senses. The common association of homosexual and psychoneurotic characteristics adds to the complexity. *Cure* is not a precise entity which can be set out by measure. And is homosexuality constitutional or acquired? Here again we have no settled body of knowledge. Havelock Ellis [9] regards "this fundamental abnormality usually called sexual inversion" as probably inborn. Freud [10] considers the question to be "fruitless and inappropriate". Feelings run high when the claims of the constitutional and fixation theories are discussed, particularly if the emotions are involved consciously or unwittingly. Stoller [11] adopts a wiser attitude: "Those who regard homosexuals as purely constitutional, as well as those who consider homosexuality as purely of psychogenic origin, are over-simplifying an extraordinarily complex subject."

III.—Homosexuality is probably as common amongst women as amongst men, but it is less prominent and it has been given less attention. In the world of affairs masculine standards largely prevail. Women can compete in public life on equal terms with men, but they are expected to keep their femininity in the background.

The homosexual is forced to seek the society of homosexuals or to live emotionally alone. The heterosexual may choose his sexual isolation—the homosexual may not. For homosexuals whose standard of life is high this isolation brings inevitably a sense of remoteness, sadness and indignation, particularly when they see that society is willing enough to accept what they contribute to the cultural values in life. The utter loneliness of the homosexual is a real thing. Our greatest service to him (or her) and to ourselves is to increase knowledge which will bring a change in educated opinion. If more than 25% in a group of educated separate classes is of fundamental importance in understanding the problem of homosexuality. Clinically, the more important although rarer type of sexual inversion is the congenital or endocrinic. Of the male congenital invert it has often been said, following Ulrichs (1864), that he possesses "a female soul in a male body". Havelock Ellis restricted the use of the term homosexual to this class alone, and in his later years (1933) he came to regard homosexuality as an anomaly, or variation of the normal sexual pattern, rather than as a perversion or a vicious moral disease. "Congenital sexual inversion is an anomaly, an inborn variation of which we are beginning to understand the causes; it is, even when extreme, only pathological in the same sense as colour-blindness or albinism or transposition of the viscera is pathological."

Among Continental workers in the same field, there has been a progressive shift of opinion away from views such as those of Charcot and Magnan (1882) that inversion is "an episode in a more fundamental process of hereditary degeneration, comparable with morbid obsessions such as dipsomania and kleptomania", and of Krafft-Ebing who, in his earlier writing (1879), considered inversion to be "a functional sign of degeneration, a partial manifestation of a neuropathic and psychopathic state which is in most cases hereditary". The latter author, in the last edition of his work (1900), was inclined to regard inversion as being "not so much a degeneration as a variation, a simple anomaly", an opinion which approximated closely to that which had long been held by inverts themselves, while with Magnus Hirschfeld (1914) "the pathological conception of inversion has entirely disappeared; homosexuality is regarded as primarily a biological phenomenon of universal extension, and secondarily as a social phenomenon of serious importance". (Havelock Ellis "Sexual Inversion", 1929, pp. 68-74.)

Concomitant with this change of viewpoint regarding the underlying pathology, or rather physiology of this clinical entity, doubts have been expressed regarding not only the efficacy but even the desirability of treatment of these cases of inborn or natural homosexuality. On this point Havelock Ellis has given his opinion that not only is treatment useless from the point of view of changing the sexual outlook of the patient, but it is indeed morally questionable whether the attempt should ever be made to interfere with the natural proclivities of an invert. The endeavour to change the character of an endocrinic homosexual into that of a heterosexual is, in the opinion of some, as futile and as unjustifiable as to seek to suborn a heterosexual to follow unnatural vice. It would appear that the moral outlook of the true invert is a thing that must be accepted, and reconciliation of the conflicting claims of society and the individual, as regards natural homosexuality, can be effected only by a change in the attitude of society toward those of their number who share this anomaly, rather than by attempting to treat by medical means a condition that is virtually unalterable. There can be no question of asking the invert to accept the ordinary standards of heterosexual morality, and any course of therapy which seeks to reverse the fundamental pattern is not only foredoomed to failure, as all the reported cases testify, but is also quite indefensible when regarded in the light of absolute morality: attempted "treatment" or alteration of the basic personality of an inborn homosexual can only be described as a moral outrage.

There are, nevertheless, certain other aspects of fundamental importance which cannot be left unexamined. The question of moral and legal responsibility may not be evaded, merely by simple disclaimer. But the problem of reconciling the demands of the law with the personal rights of the abnormal but not vicious individual is not so difficult as would at first sight appear. Leaving aside the private relations of adult homosexuals one with the other, with which outside society can have no moral justification for interfering, the only offence other than blatant indecency that can properly come within the ambit of the aspect of such an investigation as here suggested to inquire—with the assistance of material drawn from suitably selected countries—whether the fact that the social stigma is much less pronounced for women than for men may not in part be due to the absence of legal penalization. Is it not conceivable that, in the course of time, indignation and stigma would be greatly reduced if the legal ban were lifted? To conclude this part of my argument: If the factor of moral indignation is seen in its true perspective, there are no adequate reasons left why homosexual activities should be regarded as anti-social and be punished, unless they involve the corruption of young people or are committed for financial gain or so as to endanger public order. A reform of the present law on such lines, in conformity with the laws of Switzerland and Poland, seems to be desirable. The argument that homosexual activities mean biological waste and should be punishable in the interest of a constructive population policy goes too far and would equally justify the penalization of masturbation, voluntary childlessness and of many forms of birth control.

(*b*) The suggested legal reform might be opposed on the ground that the exceptions for which punishment should in any case be retained would prove so much more frequent than the rule that the reform might not be worth while. This point is obviously a purely factual one on which further statistical information should, and could, be collected by analysing a substantial number of court cases. Special attention should be paid to the following points: age of the parties concerned; their social and family status; their financial relations; circumstances and locality of the offence; formation of social and anti-social groups of homosexuals and their activities, particularly the relation between homosexuality and other, sexual and non-sexual, offences; relation between frequency of homosexual offences, on the one hand, and sex ratio and political structure of the community, on the other.

(*c*) The effect of imprisonment and other types of institutional treatment of offenders, sexual and others, has to be carefully studied. Information on the matter is available mainly from American sources, e.g. Donald Clemmer, "The Prison Community"; Joseph Fishman, "Sex in Prison": "homosexuals who go to prison and homosexuals who are made in prison". Estimates of the actual extent of the evil in institutions of this kind and views on the part played by the factor of detention in the causation or evolution of homosexual tendencies differ widely. In this country, non-official students of the problem have to rely on books by ex-prisoners as the almost only source of information, and an extension of the fact-finding inquiry to this side of the matter—difficult though it will be—seems desirable. Even if the law should be reformed, the problem itself, though on a somewhat smaller scale, will remain since many homosexuals will still be sent to prison for non-sexual offences and some even for homosexual ones. Can nothing be done to relax the sexual strain in penal and reformatory institutions? In Mexico and Brazil, women are permitted to enter the prisons for this purpose, whereas in Columbia well-behaved prisoners may leave the prison twice a month under escort on a sexual visit (see the most recent information in Professor Negley K. Teeters, "Penology from Panama to Cape Horn", 1946, who recommends the second system, with suitable modifications for the U.S.A.). Even if this should not appeal to people in this country, at least in Approved Schools and similar institutions some relaxation of the sexual tension might be achievable by permitting more social contact between the sexes, carefully graded according to age and psychological characteristics. In this direction, too, some further research may well be indicated.

Dr. D. Stanley-Jones: Several schemes for the classification of homosexuality have been suggested, of varying degrees of complexity, and in nearly all there is a division into major groups, that are variously referred to as congenital and acquired, organic and functional, physiological and psychological. The recognition of these quite and primitive kind of sexual outlet, and a large proportion of the men showed other sexual perversions which suggested that a personality factor was present. There seems to be a specific inherited tendency towards homosexuality sometimes. The most important environmental factor in the series was early seduction by homosexual men. More general causes are the racial and social conditions which tend to favour it. Some men temporarily adopt this means of gratification when circumstances prevent heterosexual relations, others when satiated with heterosexual experiences. Many confirmed homosexuals are perfectly potent in normal sexual relations with women. Among adolescents it is often a transitory experience and many adolescent male prostitutes are not true homosexuals and easily give it up. The tendency towards homosexual interest may be first realized at any age, and its overt expression may be released by alcohol, senility, and other mental conditions associated with loss of control. There is no reason to believe that the homosexual urge is stronger than the heterosexual. But the problems of the chaste homosexual may be particularly difficult and complicated. The suggestion that the association of other perversions with homosexuality is due to the fact that homosexuals are a persecuted class and tend to associate with those who are condemned for other reasons is probably only relatively true, since the ordinary offender holds the homosexual in contempt. Moreover, among women homosexuals, in whom the social ban is less significant, other sexual deviations are more frequent than in women of normal sexuality.

Imprisonment, even without psychotherapy, may have a curative effect, but is sometimes ineffective. Psychotherapy as an adjunct to a sentence of imprisonment has a place in the treatment of specially selected cases. Favourable indications for treatment are youth, good personality, a first offence, absence of habit, a real anxiety accompanying overt behaviour, sincerity of co-operation, and good physical and mental health which assists in preventing the release of homosexual activity. It seems necessary that homosexuality in men must be penalized if it leads to the debauching of young people, if it offends against public decency, if it is carried out for monetary gain, or if the homosexual is in any public place for the purpose of prostitution or solicits to the annoyance of passengers.

Dr. John C. Mackwood: The cases that come to my notice in Wormwood Scrubs Prison are selected ones; all these are seen by me though not all are further treated. They are by no means a medical selection for many come through a direction or recommendation of the Courts. Thus a number of cases are treated that otherwise would not have had precedence had a clinical or optimum selection alone been the criterion. Whilst clinical evidence of anxiety-tension is the main indication for treatment some of the over-dependent, separation-anxiety types and certain personality types with little control over the volume of diffuse feeling—"nostalgic" personalities describes them fairly aptly—tend to find psychotherapy too challenging. These individuals are apt to surrender too much to their self-pity and masochistic trends, and cannot face the further release of anxiety under treatment. But they are more than balanced by others who find—when they can no longer retreat from their problems—that they get relief from psychotherapy; and many of these appear to do better than outside prison—certainly the tempo of their progress is often much higher. One finds many cases that have started treatment outside before conviction and broken off of their own accord who do well in prison, and some who have avoided it when it has been advised and available outside prison to take to it with benefit inside. The preponderating number of convicted homosexuals and those for sexual offences of other kinds are of minor degree.

One is primarily struck by the *immaturity* of the *emotional* development of these individuals. In the general run of cases it is not so much the homosexuality that is stressed as the immaturity, and the homosexual content is a symptom of the general law is the sexual seduction of young persons. Now it is a matter of experience that this particular type of offence is rarely committed by the natural invert, whose affections in the first place almost invariably go out toward an adult of his own sex, in exactly the same way as the desires of a normal heterosexual are directed toward an adult, a potential mate, rather than toward a child. The seduction of children bears no direct relation to homosexuality as such, but may properly be called an anti-social perversion, regardless of whether the offence is heterosexual or homosexual. The law quite rightly makes a distinction between heterosexual intimacy between adults and with adolescents, regarding the latter as an anti-social and therefore a criminal offence necessitating segregation; but in the matter of homosexual activity no such distinction is drawn, and the satisfaction of private sexual desires between like-minded adults is classed equally with unnatural offences against children [1]. This attitude runs counter to all considerations of psychology and common sense.

Acquired, functional, or psychological homosexuality falls within an entirely different category from that of true homosexuality. By far the greater number of wrongdoers who are actually charged with homosexual offences are not natural inverts in the medical sense of the term, but merely immature heterosexuals or bisexuals; as a result, the reasonable claim of *bona fide* inverts to a just recognition of their rights as a social minority is gravely prejudiced by the actions of others who in no way can join in this claim, but who by popular misconception and in the eyes of the law are grouped indiscriminately with true homosexuals as criminally minded perverts.

From the therapeutic point of view, moreover, the distinction is amply justified, and the trend of advanced medical thought is in the direction of educating legal and administrative opinion toward a complete separation of the two categories, the true homosexual being rescued from the clutches of a law which sometimes operates with mediæval barbarity [2], and which serves no useful purpose other than to make easy the lucrative calling of the blackmailer, while offenders against young persons, be they heterosexual or homosexual, are regarded as being more in the nature of psychopaths who need and who can respond to suitable therapy.

The psychogenesis of the pseudo-homosexual has been given at length elsewhere [3], and reasons have been adduced for believing that the persistence into adult life of the homosexual tendencies that are natural and indeed universal during adolescence is symptomatic of a failure of development, an arrest of normal psychological growth at the pre-adolescent stage of homosexuality, rather than of the emergence of inborn and unalterable traits that inform the basic pattern of an abnormal personality. From the point of view of treatment the difference is of supreme importance, for in contradistinction to the endocrinic type that is impervious to any form of therapy, the acquired type of homosexuality yields to psychotherapeutic measures, usually with success and often resulting in a complete cure.

REFERENCES

1 Stanley-Jones, D. (1946) Sexual Inversion and the English Law, *Med. Pr.*, **215**, 391.
2 —— (1946) Homosexuality, *Brit. med. J.* (i), 179.
3 —— (1947) Sexual Inversion: An Ethical Study, *Lancet* (i), 366.

Sir Norwood East: It may be misleading to compare homosexuality in the two sexes. Murder and attempted murder are not uncommon results of male homosexuality and are sometimes due to jealousy, but I cannot recall a crime of this type—other than a suicide pact—occurring in women. It is sometimes suggested that as homosexuality in women is not illegal it is unnecessary to penalize it in men. But women lawyers and doctors with special experience of such cases appear to be alarmed at its increase in women to-day. It is convenient to regard homosexuality as being constitutional or acquired. It is usually due to a combination of factors. In a series of 79 homosexual offenders there was a general tendency toward a varied

Section of Anæsthetics

President—Stanley Rowbotham, M.D.

[*April* 11, 1947]

DISCUSSION ON FURTHER EXPERIENCES WITH CURARE

Dr. Frederick Prescott (*in absentia*, read by **Dr. R. H. Roberts**): *Some aspects of the clinical pharmacology of curare.*—Curare is a crude plant extract obtainable from a number of species of tropical liane; it is of varying composition and totally unfit in its crude state for clinical use. It contains a number of alkaloids, some of which paralyse skeletal muscle by a myoneural block, others with a central convulsant action, and others with a lissive or relaxing action on spastic muscle. It is therefore incorrect to use the term curare when referring to a preparation employed to block neuromuscular conduction. Clinically the only alkaloid of interest in preparations of curare is *d*-tubocurarine chloride, which is occasionally misnamed curarine, which is quite a different alkaloid. In clinical doses *d*-tubocurarine chloride has practically no action other than the property of paralysing skeletal muscle by blocking conduction at the myoneural junction.

Two preparations obtained from crude curare are available for clinical use. One is *Intocostrin*, a purified curare extract obtained from the South American liane *Chondrodendron tomentosum*. This preparation owes its curariform action, i.e. ability to produce a myoneural block, almost entirely to the *d*-tubocurarine chloride present. Pure *d*-tubocurarine chloride is available stabilized as a solution containing 10 mg. per ml. under the name Tubarine. Both intocostrin and *d*-tubocurarine chloride are free from the undesirable side effects of some of the alkaloids in crude curare. Intocostrin is standardized in units of a standard preparation of curare (0·02 gramme per ml.) and not by its content of *d*-tubocurarine chloride. This has sometimes caused some confusion in dosage when changing from one drug to the other. Assayed by the rabbit head-drop crossover method 6·67 units of intocostrin are equivalent in activity to 1 mg. of pure *d*-tubocurarine chloride. There is some difference of opinion, however, whether this ratio holds in clinical practice. I have always considered that clinically the ratio is more like 3·0 to 3·3 units of intocostrin to 1 mg. of the pure alkaloid, but it is difficult to make an exact comparison in anæsthetized subjects, as one cannot be certain of the part played by the anæsthetic and one has no absolute measurement of relaxation in the unconscious subject.

There have been many conflicting statements made on the pharmacology of curare preparations. This is because sometimes a preparation of unknown potency and composition has been used and has been referred to as "curare", sometimes the writer has used intocostrin and sometimes *d*-tubocurarine chloride; moreover the experimental animals have included all those found in the pharmacological laboratory as well as man; the dosage has varied enormously; sometimes the drug has been given with an anæsthetic, and sometimes without; and the route has varied. Little wonder is it that statements on "curare" are so contradictory.

d-Tubocurarine chloride belongs to a group of compounds known as quaternary ammonium salts, which, in general, exhibit the property of paralysing neuromuscular conduction at the myoneural junction. According to Gross and Cullen (1945) the curariform neurotic personality disorder. For instance, all these individuals are philanderers and this is their greatest risk, for they involve each other in a high percentage of cases that come to prison. But this philandering is itself a sign of immaturity and is not essentially different from the philandering of the immature heterosexual.

These immature personalities, in selected cases, respond well to treatment in prison.

Difficulties and disadvantages in prison.—There are a considerable number of handicaps to treatment in prison that are inherent in the build-up of the machinery for holding prisoners during their sentence. One of the greatest of these is lack of space, outside the cells, for the outlet of energy in a healthy manner. Another is the obvious drawback of the many hours of isolation for the isolated personalities.

One of the greatest improvements has been the building of a New Ward—we have carefully avoided calling it a *psychological* ward, and we term the cases under treatment *exploratory* cases—where all kinds under treatment live and sleep together. It is an asset of the utmost value and has enabled us to start Group Treatment. When cases under treatment can be observed closely in the ward and in relation to each other, both in and out of the Group Session, there are obvious advantages: one has treatment and observation *in vivo* rather than *in vitro*, and the duller mentalities can respond to concrete situations in a way that they would be unable to do with the more abstract and introspective methods of treatment.

Prison is not only a potentially homosexual atmosphere but also a very definitely actual one, where one gets many homosexuals migrating into groups. It might be thought that this would operate unfavourably in treatment, but one finds in practice that the homosexual element in a group does not weigh it down. I have one such Group Treatment with 5 homosexuals out of 9, and it is the homosexuals who are most often at variance in the subjects that crop up—and in a healthily aggressive manner.

The signs of improvement that appear to be reliable are the following: (1) The individual mien and bearing of the prisoner and his behaviour generally to the prison regime. (2) The inter-relations of the individual to the other members of the group. (3) The liberation of energy. This is often quite outstanding and is extremely difficult to provide with a suitable field for its healthy motor discharge.

We are able to send many men out of prison with a new orientation and wanting to face up to life in a realistic manner. Follow-ups are obviously extremely difficult for the discharged prisoner wants his prison history to be a sealed book.

On this social aspect of the problem an interesting point emerged in a Group discussion. It was the opinion of a mixed group, under treatment, that of the hardships in prison life: Around 70% could be attributed to the treatment of prisoners by prisoners. Around 25% were due to the routine prison regimen. Around 5% were due to the personality difficulties of the Warder Staff.

In untreated prisoners I think the allocation would be into three more or less equal categories. So that the difference in treated cases is highly significant. This is a tribute to the prison staff at Wormwood Scrubs. But the outstanding significance of this allocation is the treatment of man by man, and it goes right to the heart of the social problem. It is still all too true that many a prisoner finds his real punishment begins after his discharge from prison. Society throws up these cases and it must be willing to find a place for them.

Many things point to the necessity for the Prison Commission to start a Social Welfare Service operating in the prisons and providing for the prisoner from the day he goes outside. Important as it is for the man to get regular work, I think the provision for his leisure life is equally important in preventing his return to prison. It is all too easy for him to drift back to his undesirable acquaintances.

a sense of choking and shortness of breath, although controlled respiration was given throughout the experiment. There was no loss of consciousness, no clouding of the sensorium, no change in visual acuity and smell. The sensations of pain and touch were normal, memory was unimpaired and the electro-encephalogram and electrocardiogram were unaffected. It was, therefore, concluded that *d*-tubocurarine chloride has no significant central stimulant, depressant or analgesic action in man. These observations confirm those of Kellgren *et al.* (1946) and Prescott *et al.* (1946). It would appear from this that the unconsciousness produced in surgical patients by Whitacre and Fisher (1945) by injecting very large doses of intocostrin was due to anoxia.

According to Cole (1946) and Perlstein and Weinglass (1946) there is a lethal dose of intocostrin even under controlled respiration. In experiments on dogs Cole found that the fatal non-anoxic dose was 23·3 units per pound; this is far greater than would ever be used clinically (maximum 0·7 unit per pound). He states that such large doses affect the cardiovascular system and produce a fall in blood-pressure, although Gray (1946) states that *d*-tubocurarine chloride, even in large doses, has no effect on the cardiac output or venous pressure in the dog heart-lung preparation. The cause of death in the dogs was obscure, but it was probably not due to any interference with oxidation systems in muscle or nerve (Featherstone and Gross, 1947). In man intocostrin and *d*-tubocurarine chloride appear to have no effect on the cardiovascular system in clinical doses. Anæsthetic deaths due to intocostrin and *d*-tubocurarine chloride have been reported, but post-mortem findings have been published in only one case. In two cases death occurred several hours after the injection, and in both of them there was massive pulmonary collapse.

Do curare-like drugs cause bronchospasm? West (1935) refers to bronchospasm in dogs produced by a curare extract of unknown origin, and Cole (1946) reported difficulty in inflating dogs immediately after injecting large doses of intocostrin. A histamine effect on the bronchi cannot be excluded, as Comroe and Dripps (1946) have described the formation of histamine-like wheals after injecting intocostrin and *d*-tubocurarine chloride intracutaneously in man, and the production of histamine has also been observed after the injection of *d*-tubocurarine chloride into animals (Schild, 1947). I believe there is a danger of bronchospasm in man if the patient is lightly anæsthetized or conscious, and if the dose of the curarizing drug is on the low side, e.g. 15 mg. *d*-tubocurarine chloride. I have seen it occur in a conscious volunteer injected with this drug and in three mental patients who were very lightly narcotized with pentothal. The most effective treatment in these three cases was to administer more pentothal or more *d*-tubocurarine chloride.

In the dog it is stated (Gross and Cullen, 1945) that *d*-tubocurarine chloride causes relaxation of the smooth muscle of the small intestine, due in part to a direct action on the effector cells of the muscle. In the patient submitted to surgery the effect of the drug cannot be separated from that due to the drugs used for premedication and anæsthesia. In operations under cyclopropane or gas and oxygen supplemented by a curarizing agent the gut appears contracted (Griffith, 1945; Prescott *et al.*, 1946), but Gray (1946) states that with barbiturate anæsthesia this does not often occur.

d-Tubocurarine chloride and intocostrin are rapidly metabolized after administration. Some of the drug is excreted by the kidneys, either unchanged or in a form still capable of curarizing. Urine obtained within an hour or so after the administration of 30 mg. of *d*-tubocurarine chloride in man has a curarizing action. This rapid elimination suggests that slow administration by an intravenous drip is unsatisfactory. This has been confirmed by slowly administering a curarizing dose of *d*-tubocurarine chloride (30 mg.) to a volunteer over a period of half an hour (1 mg. per minute). Paralysis was incomplete, and ten minutes after receiving the drug the subject was able to sit up. The same dose given rapidly intravenously produced respiratory paralysis (Prescott *et al.*, 1946). If curarizing drugs are given by an intravenous drip a dose sufficient, or nearly sufficient, to curarize must be given; then curarization may be maintained by the drip. There is some difference of opinion whether a curarizing dose of drug should be given all at once intravenously owing to the danger of respiratory paralysis. A committee appointed by the Medical Research Council suggests that not more than 10 to 15 mg. of *d*-tubocurarine chloride should be administered at once and that after a pause to observe the effect on respiration another dose can be given subsequently. Some authorities, e.g. Gray and Halton (1946) and Knight (1946) recommend the use of fractional doses of a curarizing drug and a barbiturate, which are given intermittently throughout the operation. It should be remembered that the buffered solution of *d*-tubocurarine chloride cannot be mixed together with a soluble barbiturate in the same syringe as precipitation occurs. Two separate syringes must be used.

There is just one further pharmacological property of intocostrin and *d*-tubocurarine chloride that is of clinical interest: they both produce salivation. It is therefore advisable drugs act anywhere in the nervous system where acetylcholine is the chemical mediator. The paralysing action of the preparations used clinically is relatively brief as they are rapidly eliminated or destroyed. In man the order in which the muscles are affected after curarization is, as Lucas points out, in the order of their phylogeny. The muscles supplied by the cranial nerves are affected first (face, neck), then those of the limbs, back muscles, abdomen, intercostals, and finally the diaphragm. After intravenous administration an effect on the eye muscles can be perceived within a minute, but the peak of curarization occurs in three to five minutes. If respiratory paralysis is going to occur it will do so within 7-10 minutes of intravenous injection. Recovery of muscle function occurs in the reverse order to which it is lost. After therapeutic doses the limbs can be moved after 30-45 minutes, but residual paralysis of the ocular muscles, causing ataxia, may last for several hours. Patients who have had curare-controlled electrical convulsion therapy appear to recover more rapidly, e.g. they can walk an hour afterwards (Hobson and Prescott, 1947).

The curariform action of intocostrin and *d*-tubocurarine is reversed by prostigmin and eserine, and also in the isolated muscle by washing out with saline. In man I have never been impressed with the action of prostigmin as an antagonist of curarizing drugs in the doses recommended, i.e. 1 to 2 mg. According to Dr. Trevan (personal communication) the action of 30 μg. of *d*-tubocurarine chloride is reversed by 10 μg. of prostigmin in the guinea-pig. If a comparable ratio applies to man at least 10 mg. would be required to reverse the dose of *d*-tubocurarine chloride that produces diaphragmatic paralysis. Cole (1946) in his experiments on dogs was unable to reverse the effect of large doses of intocostrin with prostigmin. Ephedrine is said to potentiate the action of prostigmin (Koppanyi and Vivino, 1944), but this has not been confirmed in man. It is also necessary to give atropine when prostigmin is administered to prevent the stimulating action of the latter on the parasympathetic nervous system. It is an apparent paradox that acetylcholine and prostigmin can, in high concentrations, exert a curariform effect and that curare-like drugs can, under certain conditions, produce muscular contraction (McIntyre and King, 1943).

The antagonism of curariform drugs and prostigmin would be easy to understand if it could be shown that the former could increase the activity of cholinesterase, the enzyme that hydrolyses acetylcholine. The literature on this is most conflicting, the bulk of the evidence suggesting that *d*-tubocurarine chloride has a slight inhibiting action on cholinesterase (Harris and Harris, 1944). Curare-like drugs form a block at the myoneural junction possibly by combining with the receptor substance in the muscle. They do not interfere with the production of acetylcholine.

Acetylcholine appears to be a chemical mediator necessary for the transmission of nerve impulses through the ganglia of the autonomic nervous system, and the view is now held that, in the experimental animal at any rate, curariform drugs are capable of acting anywhere in the nervous or muscular system where acetylcholine is the chemical mediator. There is also evidence that they block peripheral response to vagal stimulation (Mautner and Luisada, 1941).

That ether has a curariform action was noted as far back as 1914. This was confirmed in 1943 by Gross and Cullen, who showed that ether intensified the action of *d*-tubocurarine chloride in the dog. They also showed that pentothal had a curariform action, but only in very high blood concentrations. Clinically it is important when giving curare-ether anæsthesia to limit the dose of the curarizing drug to one-half to one-third that used with other anæsthetic agents.

There is considerable difference of opinion on the effect of curare-like drugs on the central nervous system in animals. Crude preparations used in the earlier studies apparently had a convulsive action on the cerebrospinal axis. Fegler (1942), employing crude curare preparations in anæsthetized dogs, concluded that curare first stimulates and then depresses the respiratory centre, and Cohnberg (1946), using a number of animals, states that *d*-tubocurarine chloride and intocostrin stimulate the central nervous system in a number of species and produce convulsions in rats. According to Pick and Unna (1945) the dose of *d*-tubocurarine chloride just sufficient to paralyse the skeletal muscle of the frog has no effect on the electro-encephalogram, although a larger dose (4 mg./kg.) does; they suggest that the drug blocks the synapses of the central nervous system. More recently McIntyre *et al.* (1946) claimed that *d*-tubocurarine chloride in doses insufficient to abolish respiratory movements produced central depression in dogs as shown by the electro-encephalogram. An experiment was recently performed on a human volunteer given 75 mg. of *d*-tubocurarine chloride over a period of forty-five minutes (Smith *et al.*, 1947). This dose is two and a half times that likely to produce complete respiratory paralysis. The subject was given artificial respiration immediately so that any effects produced could not be attributed to anoxia. The blood-pressure and pulse-rate underwent no significant change. There was, however, I have found tubarine valuable in the relief of *laryngeal spasm* but the dose which will produce the ideal result of quiet spontaneous breathing is variable. Roughly, an adult will need 10 mg. in the first plane of the third stage of anæsthesia and 5 mg. in the second plane.

I anæsthetized a tall red-headed young man for a sublabial antrostomy. He had a healed tuberculous focus in the apex of the right lung and a basal bronchiectasis following influenzal pneumonia three years previously. He produced 2 drachms of sputum daily. He had, also, a high arched palate, protruding teeth and an underslung lower jaw. Pentothal 1 gramme failed to relax his jaw, so cyclopropane was added. Attempted laryngoscopy produced severe laryngeal spasm which made it impossible to give more cyclopropane. Tubarine 10 mg. intravenously gave immediate relaxation of the cords and chest wall and he started to breathe quietly. Laryngoscopy was achieved with some difficulty, he was intubated and his trachea sucked out at leisure before continuing. There were no further complications during operation or recovery.

I gave another man, weighing 175 lb., pentothal 0·5 gramme followed by nitrous oxide, oxygen and ether. He moved at a premature incision. Rushed introduction of ether caused much coughing and a persistent stridor which would not respond to any of the usual remedies. After twenty minutes, with anæsthesia in the second plane, I injected tubarine 5 mg. into the external jugular vein. He was quiet in twenty-five seconds, with shallow breathing and a tendency to cyanosis. Tracheal tug was well marked from ten to twenty minutes afterwards. There was an expiratory wheeze, probably bronchial, from twenty-two to twenty-seven minutes and at thirty-one minutes stridor returned.

Tubarine does not always prevent laryngeal spasm.

I gave a man, aged 56, pentothal 1 gramme and tubarine 10 mg. He was not apnœic. Attempted nasotracheal intubation with a laryngoscope (he was edentulous) produced severe laryngeal spasm and some cyanosis. This was relieved by spraying cocaine on to the cords down the laryngoscope. Although the cords were in spasm, the pharynx and jaw were well relaxed and I had an excellent view.

I have noticed frequently that where tubarine is used with pentothal there is less tendency to apnœa than would have been expected with the same dose of pentothal alone. I wondered whether the effect of pentothal might be due not merely to medullary depression but to an active reflex inhibition of respiration which is prevented by the tubarine.

I have previously decried [1] the use of tubarine for bronchoscopy and œsophagoscopy but I must retract. Bronchoscopy is made to look easy at the hands of the relatively inexpert. Œsophagoscopy with pentothal alone is a dangerous operation owing to the difficulty of maintaining a clear airway. With tubarine as well I have had no anxiety. The airway remains clear and the patient breathes quietly. The passage of the œsophagoscope through the relaxed pharyngeal sphincters is made much more easy and therefore, I think, less traumatic. I use, in adults, tubarine 15 mg. with pentothal as required, the dose varying from 0·4 to 1 g.

The effects of tubarine on the *cardiovascular system* are not quite clear to me. The skin vessels are commonly dilated, the face is often seen to be flushed and bleeding is increased. Pallor is not a common accompaniment of blood-pressure fall but I have once noted it in a man with normal blood-pressure.

From a group of blood-pressure charts I found a serious drop (systolic at 80 mm.Hg or less at the end of operation) in seven. These included an excision of rectum, two prostatectomies, one hysterectomy, an amputation through the hip-joint accompanied by severe hæmorrhage, and two upper abdominal operations, in one of which the pre-operative pressure was only 90/50. In 17 the blood-pressure remained steady. One was an amputation through the thigh, 6 were operations in the lower abdomen including 3 colectomies, and 10 were upper abdominal. 11 showed a rise in blood-pressure at the end of the operation, all upper abdominal. One of 7 in the first group, 7 of 17 in the second and 8 of 11 in the third were on carbon dioxide absorption, suggesting that deficient absorption may have been a factor. On the other hand, the rising proportion of upper abdominals may mean that curarization was more complete and tidal volume of respiration less adequate.

It has been suggested, and I have thought myself, that the steadiness of blood-pressure and pulse-rate in upper abdominal operations must be due to some protective action of curare against noxious stimuli. On the other hand, good muscular relaxation gives good access and trauma may be negligible. Equally good results may be had with pentothal, nitrous oxide and intercostal nerve block without splanchnic block.

Surgical stimuli can, undoubtedly, produce a cardiovascular reaction. In abdominal operations the usual form is that of blood-pressure fall accompanied by slowing of the pulse. In one gastrectomy operative stimuli overcame the depression caused by a relative overdose of opiates with pentothal. The blood-pressure stabilized at 20 mm.Hg. above the pre-operative level.

I have found, almost invariably, a fall in blood-pressure with retropubic prostatectomy, in one case to a level far below any I have seen in a similar operation. (A rise occurred within a few minutes of the intramuscular injection of ephedrine ½ grain.) The fall may accompany or follow the enucleation. In one case the pulse fell from over 80 to round 40 for 35 minutes (pentothal 0·35 gramme followed by nitrous oxide and ether: no clinical anoxæmia); four hours later there was pulsus alternans with a regular rate of 100. In another case the enucleation was anticipated with a further injection of pentothal; here the fall was less marked.

for the patient to be atropinized (atropine sulphate, gr. 1/100 to 1/50) if these drugs are given. In the case of patients undergoing curare-modified electrical convulsion therapy the atropine is given intravenously at the same time as the curarizing drug (Hobson and Prescott, 1947).

Finally there is one maxim to be followed whenever a curarizing drug is used: Keep the patient breathing.

REFERENCES

COHNBERG, R. E. (1946) *J. Lab. clin. Med.*, **31**, 866.
COLE, F. (1946) *Anesthesiology*, 7, 190.
COMROE, J. H., and DRIPPS, R. D. (1946) *Anesthesiology*, 7, 260.
FEATHERSTONE, R. M., and GROSS, E. G. (1947) *Amer. J. Physiol.*, **148**, 507.
FEGLER, J. (1942) *J. Physiol.*, **100**, 417.
GRAY, T. C., and HALTON, J. (1946) *Proc. R. Soc. Med.*, 39, 400.
GRIFFITH, H. R. (1945) *Canad. med. Ass. J.*, **50**, 144.
GROSS, E. G., and CULLEN, S. C. (1943) *J. Pharm. exp. Therap.*, 78, 358.
—— (1945) *Anesthesiology*, 6, 231.
HARRIS, M. M., and HARRIS, R. S. (1944) *Proc. Soc. exp. Biol. Med.*, 56, 223.
HOBSON, J. A., and PRESCOTT, F. (1947) *Brit. med. J.* (i), 445.
KELLGREN, J. H. *et al.* (1946) *Brit. med. J.* (ii), 898.
KNIGHT, R. J. (1946) *Canad. med. Ass. J.*, **55**, 356.
KOPPANYI, T., and VIVINO, A. E. (1944) *Science*, **100**, 474.
MCINTYRE, A. R., and KING, R. E. (1943) *Science*, **97**, 516.
—— *et al.* (1946) *Fed. Proc.*, **5**, 67.
MAUTNER, H., and LUISADA, A. (1941) *J. Pharmacol.*, 72, 386.
PERLSTEIN, M. A., and WEINGLASS, A. (1946) *Amer. J. dis. Child.*, 67, 360.
PICK, E. P., and UNNA, K. (1945) *J. Pharm. exp. Therap.*, 83, 59.
PRESCOTT, F. *et al.* (1946) *Lancet* (ii), 80.
SCHILD, H. O. (1947) To be published.
SMITH, S. M. *et al.* (1947) *Anesthesiology*, **8**, 1.
WEST, R. (1935) *Proc. Roy. Soc. Med.*, 28, 565.
WHITACRE, R. J., and FISHER, A. J. (1945) *Anesthesiology*, 6, 124.

Dr. Geoffrey Organe: *Further experiences with* d-*tubocurarine chloride.*—Some years ago I produced a number of case records carefully selected to show that perfect results could sometimes be achieved in spite of prolonged anæsthesia. To-day my records are selected to show that the results of using *d*-tubocurarine chloride in anæsthesia are not always all that could be desired. I do not want to convey the impression that I would wish to abandon its use, particularly as Dr. Prescott and I did the first experimental work on the preparation now known as tubarine. I do feel, however, that our early clinical reports have been coloured with roseate enthusiasm.

My equanimity was first disturbed by the development of what seemed an unduly large number of serious *post-operative chest complications.* We have followed them with some care in 86 patients having abdominal operations. It seems to be a fairly general experience that the frequency of any complication increases with the care of the follow-up. My figures must, therefore, be discounted to some extent for comparison.

There were, among these 86, 24 patients with major and 15 with minor chest complications—a sobering experience. Of the first group 12 developed lobar collapse, usually bilateral, one bronchopneumonia, one a subphrenic abscess with pleural effusion, one a pulmonary infarct and 9 a cough with fever and much sputum. I have tried to relate these to the accompanying anæsthetic agent or to the technique of its administration, without success. All are incriminated: Ether, cyclopropane, nitrous oxide, pentothal, semi-closed and closed. There seems to be no relation to the degree of respiratory depression at operation or to extreme degrees of cardiovascular depression. The only significant factor was tracheal intubation. In a group of 59 having upper abdominal operations, 11 of 15 patients intubated developed chest complications compared with 20 of 44 not intubated. The only explanations that occur to me are a tracheitis and the possibility of a reflex bronchospasm due to the presence of the tube in the trachea. I have no evidence of either. I have only once seen a patient with symptoms suggestive of bronchospasm and his recovery was uncomplicated. The incidence is higher in men than in women; it is higher, too, with upper abdominal than with lower abdominal operations. All 12 cases of lobar collapse were in a group of 36 men having upper abdominal operations.

One patient died of bronchopneumonia, one of the original disease, and one was later found to have early bronchiectasis. The others appeared, at the time of their discharge (which was not delayed in any case), to have recovered completely.

I should add that, using small doses of tubarine, we rarely assist respiration.

It is suggested by some that intocostrin is unreliable. I have used both tubarine and intocostrin in considerable quantity and still say that, dose for dose, I am unable to detect any significant difference in effect between the two substances. The effects of both vary from patient to patient according to many factors; but then so do the effects of pentothal, and many other drugs. This has to be taken into account always.

One of the most significant aspects of the advent of curarization is the possibility it offers in abdominal surgery of reducing the number of spinal anæsthetics administered. There are, however, a few operations in which spinal is still the better method as, for example, in abdomino-perineal excision of the rectum, where maximal relaxation is vital. Few anæsthetists will deny that for the degree of relaxation it produces, spinal anæsthesia is still unequalled. It is, however, attended by the serious danger of infection unlike intravenous injections. The sterility of the modern preparations of spinal anæsthetics can be relied on but a very exacting aseptic technique is called for. This is difficult for the anæsthetist to encompass in these times of shortage of nursing staffs. The hazard of other central nervous system sequelæ has been practically eliminated since the introduction of nupercaine, but the grave danger of meningitis can be readily appreciated by observing the steady increase in reported series of cases which has accompanied the great increase in popularity of spinal anæsthesia in recent years.

All now agree that the lighter the plane of anæsthesia the less the damage likely to be inflicted on the patient. Curare can be used satisfactorily in second plane anæsthesia, and sometimes even in first plane anæsthesia. Myanesin is even more advantageous in that it is usually adequate in first plane anæsthesia. Here is another advantage of curarization—the elimination of the need for deep soakings of the patient in general anæsthetics to obtain adequate relaxation.

Stress has been laid on the advantage of curare to facilitate laryngeal intubation. I have been disappointed with it in this respect. I still prefer a rapid intubation following a carefully judged dose of pentothal; for it is only when curare and pentothal combined are used in doses which to my mind are unwisely big that intubation is really likely to be facilitated. I feel that initial doses of the order of 15 mg. of tubarine plus 0·5 gramme pentothal which means in effect 15 mg. given whilst the patient is in third or fourth plane anæsthesia albeit temporarily, and which frequently produce complete *flaccid* respiratory paralysis, are not ordinarily justifiable. I have found 10 mg., or even 5, of tubarine frequently adequate as an initial dose for the production of muscular relaxation after the patient has been stabilized in light second plane anæsthesia, and these doses rarely if ever produce diaphragmatic paralysis or more than fleeting intercostal paralysis. On the other hand even 15 mg. of tubarine plus 0·5 gramme pentothal is not infrequently insufficient properly to relax the vocal cords. The same argument in equivalent doses applies to intocostrin.

A number of house surgeons have spoken to me of the shock-like state that they have to deal with on occasions following the administration of curare. Twice has this been followed by a shock-like death. The doses of curare in some of those cases were higher than I personally have found wise. I have not myself seen this condition, but I consider it may be due in great part to a profound weakness of the respiratory muscles and loss of tonus (comparable to that seen in the apparently drowned) which causes not only anoxia even with "aided respiration" owing to the loss of elastic recoil but also a deficiency in the respiratory pump mechanism which is of such importance in maintaining an efficient filling of right heart. It is for this reason that I deprecate the use of big doses of curare, such as 20 to 30 mg. of tubarine to produce spectacular results; preferring the doses 7 to 15 mg. of tubarine to produce reasonable and adequate relaxation and to keep the alternative spinal technique still in reserve for selected cases. I have not observed the shock-like state in any of my own cases. Myanesin, on the other hand, does not cause intercostal or diaphragmatic paralysis and I have not seen the shock-like state following its use, nor have the house surgeons above referred to.

SUMMARY

(1) Curarization has come to stay, and I think that myanesin will supersede curare for this purpose, because of its far greater margin of safety (the dosage of curare is agreed to be very critical) and its simple organic synthesis.

(2) Although it would be an enormous advance if the need for intrathecal injections could be entirely dispensed with, to be able to reduce them to a minimum is a great advantage.

(3) Although I very rarely use ether, I am glad that I need no longer employ third or fourth plane general anæsthesia with *any* agent.

(4) Neither curare nor myanesin seems to me to be worth while to facilitate intubation.

(5) Finally both substances need more caution in their administration than would appear to be exercised at present if a really splendid advance in the science of anæsthesia is not to run the risk of falling into disrepute.

I have anæsthetized 3 patients for amputation through the thigh with only pentothal 0·5 gramme and nitrous oxide, using tubarine to hold them on the operating table. One showed an asphyxial rise of blood-pressure, due to shallow breathing, with accompanying extrasystoles. One showed a sharp transient fall in systolic and rise in diastolic pressure at the moment of severance. All three were exceptionally well after operation.

Pulse irregularities have been not uncommon. In one prostatectomy the pulse was steady until the onset of hæmorrhage from the prostatic bed when there developed signs of a sluggish peripheral circulation, with extrasystoles—presumably due to coronary anæmia. In another patient, undergoing gastrectomy, cyanosis was accompanied by a drop in pulse-rate from 60 to 34 and back within one minute.

Pulse-rate varies but is commonly steady in spite of wide alteration in blood-pressure. It may rise or fall with blood-pressure fall. The interpretation of these varying reactions is not clear to me.

Venespasm is a common accompaniment of severe blood-pressure fall with most anæsthetic agents but is much less common where tubarine is used. In one case, although blood-pressure and pulse-rate were normal, the maximum rate of blood drip was only 40/min. Within five minutes of injecting tubarine 5 mg. the rate rose to 175/min. At the end of operation there was a severe fall in blood-pressure with change of posture. At this point, although the blood-pressure was at shock level (55/35), the blood transfusion dripped freely at 180/min.

In one patient with a low pre-operative blood-pressure (75/55) there was no change during anastomosis of the colon, lasting one hour.

There are two other cases of interest I should like to mention:

A man, aged 41, with perforated gastric ulcer, developed respiratory obstruction after pentothal 0·5 gramme and tubarine 15 mg. Attempted artificial respiration blew gas down the relaxed œsophagus through the gastric perforation into his open abdomen. Laryngoscopy showed a large piece of inspissated mucus obstructing his vocal cords. This was removed, a tracheal tube introduced, and all was well.

The other had his rectum removed and had been for nearly two hours in a steep Trendelenburg position. On the next day his pulse was 160/min., temperature 101° F. and respirations quickened. Breathing was distressed and bubbly. There was impaired percussion note and air entry at the left base, with generalized râles. Radiography showed collapse of the lower lobe with congestion on the other side. I bronchoscoped him and sucked out a lot of frothy mucus from the left side, the right being clear. There was no obvious clinical improvement and he died on the following day. At post-mortem he was found to have an acute perforated ulcer in the œsophagus with another in the stomach. Gastric contents had entered the left pleural cavity and partly digested the left lung. There was a large amount of fluid in the right pleural cavity.

If I have made it clear that, because one is using tubarine, one must neglect none of the precautions usually undertaken with major operations I have accomplished my purpose.

Many of my records have been taken, without permission, from my colleagues. The arduous task of follow-up was undertaken by Dr. Ian English.

REFERENCE

1 ORGANE, G. (1946) *Proc. R. Soc. Med.*, 39, 636.

Dr. Barnett Mallinson: *Some general aspects of the technique of Curarization.*—There are a few general points that come to my mind as a result of nearly three years' experience of the technique of curarization.

There are many methods, all with their own special disadvantages of producing muscular relaxation. The latest one seems to require a concise label. For the purpose of the present discussion I propose to refer to the "Technique of Curarization of Muscles" or more shortly just to "Curarization" when I mean the production of muscular relaxation during light general anæsthesia by the intravenous injection of either curare or substances having effects similar to it.

There seems to be little doubt that the technique of curarization has very great value and should take its place amongst the rapidly increasing resources of the anæsthetist *provided that great caution is used in the selection of cases and in the dosage and manner of administration of curare to them in these early days.* For it is early days even in reference to curare itself, whilst the new substitute myanesin is as yet in its infancy.

Using curare, one is impressed with its potency and its efficiency, but on reading and hearing about curare one is impressed with the number of deaths which have occurred: too many amongst even the few thousand administrations which can have, as yet, taken place in this country. Before adopting any new technique I made it a rule to study with an acknowledged expert and, if possible, to use it under his supervision before attempting it alone. To assure that curarization takes the place it certainly deserves—I commend this course to any colleague of moderate experience proposing to employ it for the first time.

It is suggested by some that intocostrin is unreliable. I have used both tubarine and intocostrin in considerable quantity and still say that, dose for dose, I am unable to detect any significant difference in effect between the two substances. The effects of both vary from patient to patient according to many factors; but then so do the effects of pentothal, and many other drugs. This has to be taken into account always.

One of the most significant aspects of the advent of curarization is the possibility it offers in abdominal surgery of reducing the number of spinal anæsthetics administered. There are, however, a few operations in which spinal is still the better method as, for example, in abdomino-perineal excision of the rectum, where maximal relaxation is vital. Few anæsthetists will deny that for the degree of relaxation it produces, spinal anæsthesia is still unequalled. It is, however, attended by the serious danger of infection unlike intravenous injections. The sterility of the modern preparations of spinal anæsthetics can be relied on but a very exacting aseptic technique is called for. This is difficult for the anæsthetist to encompass in these times of shortage of nursing staffs. The hazard of other central nervous system sequelæ has been practically eliminated since the introduction of nupercaine, but the grave danger of meningitis can be readily appreciated by observing the steady increase in reported series of cases which has accompanied the great increase in popularity of spinal anæsthesia in recent years.

All now agree that the lighter the plane of anæsthesia the less the damage likely to be inflicted on the patient. Curare can be used satisfactorily in second plane anæsthesia, and sometimes even in first plane anæsthesia. Myanesin is even more advantageous in that it is usually adequate in first plane anæsthesia. Here is another advantage of curarization—the elimination of the need for deep soakings of the patient in general anæsthetics to obtain adequate relaxation.

Stress has been laid on the advantage of curare to facilitate laryngeal intubation. I have been disappointed with it in this respect. I still prefer a rapid intubation following a carefully judged dose of pentothal; for it is only when curare and pentothal combined are used in doses which to my mind are unwisely big that intubation is really likely to be facilitated. I feel that initial doses of the order of 15 mg. of tubarine plus 0·5 gramme pentothal which means in effect 15 mg. given whilst the patient is in third or fourth plane anæsthesia albeit temporarily, and which frequently produce complete *flaccid* respiratory paralysis, are not ordinarily justifiable. I have found 10 mg., or even 5, of tubarine frequently adequate as an initial dose for the production of muscular relaxation after the patient has been stabilized in light second plane anæsthesia, and these doses rarely if ever produce diaphragmatic paralysis or more than fleeting intercostal paralysis. On the other hand even 15 mg. of tubarine plus 0·5 gramme pentothal is not infrequently insufficient properly to relax the vocal cords. The same argument in equivalent doses applies to intocostrin.

A number of house surgeons have spoken to me of the shock-like state that they have to deal with on occasions following the administration of curare. Twice has this been followed by a shock-like death. The doses of curare in some of those cases were higher than I personally have found wise. I have not myself seen this condition, but I consider it may be due in great part to a profound weakness of the respiratory muscles and loss of tonus (comparable to that seen in the apparently drowned) which causes not only anoxia even with "aided respiration" owing to the loss of elastic recoil but also a deficiency in the respiratory pump mechanism which is of such importance in maintaining an efficient filling of right heart. It is for this reason that I deprecate the use of big doses of curare, such as 20 to 30 mg. of tubarine to produce spectacular results; preferring the doses 7 to 15 mg. of tubarine to produce reasonable and adequate relaxation and to keep the alternative spinal technique still in reserve for selected cases. I have not observed the shock-like state in any of my own cases. Myanesin, on the other hand, does not cause intercostal or diaphragmatic paralysis and I have not seen the shock-like state following its use, nor have the house surgeons above referred to.

SUMMARY

(1) Curarization has come to stay, and I think that myanesin will supersede curare for this purpose, because of its far greater margin of safety (the dosage of curare is agreed to be very critical) and its simple organic synthesis.

(2) Although it would be an enormous advance if the need for intrathecal injections could be entirely dispensed with, to be able to reduce them to a minimum is a great advantage.

(3) Although I very rarely use ether, I am glad that I need no longer employ third or fourth plane general anæsthesia with *any* agent.

(4) Neither curare nor myanesin seems to me to be worth while to facilitate intubation.

(5) Finally both substances need more caution in their administration than would appear to be exercised at present if a really splendid advance in the science of anæsthesia is not to run the risk of falling into disrepute.

I have anæsthetized 3 patients for amputation through the thigh with only pentothal 0·5 gramme and nitrous oxide, using tubarine to hold them on the operating table. One showed an asphyxial rise of blood-pressure, due to shallow breathing, with accompanying extrasystoles. One showed a sharp transient fall in systolic and rise in diastolic pressure at the moment of severance. All three were exceptionally well after operation.

Pulse irregularities have been not uncommon. In one prostatectomy the pulse was steady until the onset of hæmorrhage from the prostatic bed when there developed signs of a sluggish peripheral circulation, with extrasystoles—presumably due to coronary anæmia. In another patient, undergoing gastrectomy, cyanosis was accompanied by a drop in pulse-rate from 60 to 34 and back within one minute.

Pulse-rate varies but is commonly steady in spite of wide alteration in blood-pressure. It may rise or fall with blood-pressure fall. The interpretation of these varying reactions is not clear to me.

Venespasm is a common accompaniment of severe blood-pressure fall with most anæsthetic agents but is much less common where tubarine is used. In one case, although blood-pressure and pulse-rate were normal, the maximum rate of blood drip was only 40/min. Within five minutes of injecting tubarine 5 mg. the rate rose to 175/min. At the end of operation there was a severe fall in blood-pressure with change of posture. At this point, although the blood-pressure was at shock level (55/35), the blood transfusion dripped freely at 180/min.

In one patient with a low pre-operative blood-pressure (75/55) there was no change during anastomosis of the colon, lasting one hour.

There are two other cases of interest I should like to mention:

A man, aged 41, with perforated gastric ulcer, developed respiratory obstruction after pentothal 0·5 gramme and tubarine 15 mg. Attempted artificial respiration blew gas down the relaxed œsophagus through the gastric perforation into his open abdomen. Laryngoscopy showed a large piece of inspissated mucus obstructing his vocal cords. This was removed, a tracheal tube introduced, and all was well.

The other had his rectum removed and had been for nearly two hours in a steep Trendelenburg position. On the next day his pulse was 160/min., temperature 101° F. and respirations quickened. Breathing was distressed and bubbly. There was impaired percussion note and air entry at the left base, with generalized râles. Radiography showed collapse of the lower lobe with congestion on the other side. I bronchoscoped him and sucked out a lot of frothy mucus from the left side, the right being clear. There was no obvious clinical improvement and he died on the following day. At post-mortem he was found to have an acute perforated ulcer in the œsophagus with another in the stomach. Gastric contents had entered the left pleural cavity and partly digested the left lung. There was a large amount of fluid in the right pleural cavity.

If I have made it clear that, because one is using tubarine, one must neglect none of the precautions usually undertaken with major operations I have accomplished my purpose.

Many of my records have been taken, without permission, from my colleagues. The arduous task of follow-up was undertaken by Dr. Ian English.

REFERENCE

1 ORGANE, G. (1946) *Proc. R. Soc. Med.*, 39, 636.

Dr. Barnett Mallinson: *Some general aspects of the technique of Curarization.*—There are a few general points that come to my mind as a result of nearly three years' experience of the technique of curarization.

There are many methods, all with their own special disadvantages of producing muscular relaxation. The latest one seems to require a concise label. For the purpose of the present discussion I propose to refer to the "Technique of Curarization of Muscles" or more shortly just to "Curarization" when I mean the production of muscular relaxation during light general anæsthesia by the intravenous injection of either curare or substances having effects similar to it.

There seems to be little doubt that the technique of curarization has very great value and should take its place amongst the rapidly increasing resources of the anæsthetist *provided that great caution is used in the selection of cases and in the dosage and manner of administration of curare to them in these early days.* For it is early days even in reference to curare itself, whilst the new substitute myanesin is as yet in its infancy.

Using curare, one is impressed with its potency and its efficiency, but on reading and hearing about curare one is impressed with the number of deaths which have occurred; too many amongst even the few thousand administrations which can have, as yet, taken place in this country. Before adopting any new technique I made it a rule to study with an acknowledged expert and, if possible, to use it under his supervision before attempting it alone. To assure that curarization takes the place it certainly deserves—I commend this course to any colleague of moderate experience proposing to employ it for the first time.

Dr. John Halton: This milestone in anæsthesia must not become a tombstone; but it will unless the physiological factors concomitant on its use are fully understood and recognized by those who employ this useful aid to anæsthesia.

Gray has shown conclusively that *d*-tubocurarine chloride, in clinical dosage, has no toxic action on the heart nor has he found there to be any poisonous effect on the liver or kidneys. It is rapidly excreted and danger lies only in its paralysant action on the mechanism of respiration. Prescott, Organe and Rowbotham, together with other independent workers, have proved conclusively that doses not exceeding 15 mg. given to a conscious patient reduce, very considerably, the tidal exchange; this fact becomes of vital importance when the subject is anæsthetized and the respiratory centre made less sensitive to stimuli. Those who employ this drug must learn a new conception of administration, it is not enough that the patient is just breathing. The respirations must be "aided" from the moment of injection until the curare effect has passed off. This may not coincide with the termination of the operation.

Intravenous thiopentone, in clinical dosage, is relatively innocuous and is rapidly eliminated but there is irrefutable evidence to show that it is a potent poison to the heart muscle in the presence of anoxæmia, with or without cyanosis. The combination of *d*-tubocurarine chloride and thiopentone without full oxygenation can therefore be extremely dangerous and is positively lethal to those in whom myocardial function is already embarrassed.

My colleague Cecil Gray and I have been using this drug, in combination with thiopentone and cyclopropane, for two years and have employed it in over 2,000 cases with but one fatal result. We believe that the secret of this form of administration lies in the following fact: These agents potentiate each other to a remarkable degree and this should be played upon, giving just as little of each one as is required to meet the surgical demands and the state of the operation.

Dr. L. O. Mountford, after hearing Dr. Gillies' report of a case of fatal bronchospasm following curare, expressed surprise at Dr. Mallinson's preference for intubating the trachea under pentothal anæsthesia, and recorded a fatal case of bronchospasm following an attempt at intubation under pentothal alone.

In order to try and eliminate such tragedies, he now cocainized the larynx and trachea prior to the use of either the curare or pentothal technique. Provided the local anæsthesia was carried out thoroughly, spasm appeared to be prevented, but inadequate local anæsthesia might be followed by spasm.

Dr. H. B. Wilson: In children I have used myanesin in a series of acute abdomens in order to obtain good muscular relaxation.

The technique employed is to give a general anæsthetic, gas–oxygen–ether, to level of lower first plane, or at most upper second plane of third stage of anæsthesia. When peritoneum is reached, myanesin is slowly injected intravenously. Relaxation comes on rapidly (usually in about circulation time) and persists for seven to twelve minutes when it passes off quite suddenly. A further dose of myanesin, usually half the initial dose, brings back relaxation for a period of fifteen to twenty minutes.

Clinically, no change has been noted in respiration or circulation following myanesin. I have had no thrombosis of veins and recovery from anæsthesia has been rapid and unaccompanied by post-operative complications.

Dr. Massey Dawkins: The benefits conferred on surgeons and anæsthetists by curare are obvious but in the case of the patient it is probable that curare does more harm than good. In a series of some 300 cases which have come under my observation, the mortality rate has been about twelve times greater than that of chloroform. In 50 gastrectomies relaxed with curare the incidence of collapse of the base of the lung, confirmed by X-ray, has been 20%. Bleeding has been excessive and I have been asked to refrain from giving curare on that ground alone by two of my surgical colleagues.

Dr. Cecil Gray: I have recently completed a careful examination of a large series of cases, and I have been able to arrive at some authoritative conclusions. I must state that with one exception I have yet to hear of any accident following the use of this drug which could be blamed on any unforeseen property or side action. In all the cases of accident which have come to my notice, including those under my care, the administrator has been at fault, not necessarily culpably for the technique of its use is still developing. This applies also to the occurrence of post-operative or indeed operative complications. The incidence of chest complications will, it is true, be high if the patient has been inadequately ventilated during the operation or if he is returned to the ward whilst still curarized.

Dr. A. C. Forrester: After using curare in some 500 cases in Glasgow, the marked improvement noticed in the general condition of severely shocked abdominal cases led me to try curare in a short series of non-abdominal shocked cases. Tubarine was used in one of these cases requiring amputation of the leg, following a street accident. This patient had been treated for shock for some hours, and although he had had two pints of plasma and one pint of whole blood, his blood-pressure would not rise above 86/68. As the limb was turning gangrenous immediate operation became a necessity. During preparation for operation in theatre, nitrous oxide and oxygen (30%) was given and the systolic pressure became stabilized at 94 mm.Hg. Within five minutes of giving 10 mg. tubarine the B.P. had risen to 120/88, and the patient left the theatre with a B.P. 115/82. He looked well and made an uninterrupted recovery. This and similar cases confirm statements made elsewhere that curare protects against shock.

If the curarization is allowed to wear off while the anæsthetic is still very light, a condition clinically resembling shock is produced. This lack of curare can be easily demonstrated by the difficulty of inflating the lungs. If more curare is given the patient's general condition immediately improves. One of my cases was a hemicolectomy. Anæsthesia was 0·5 gramme pentothal with nitrous oxide and oxygen and a trace of trilene (2 c.c. per hour given in a Rowbotham's chloroform bottle) with 20 mg. tubarine. After about forty minutes the effect of the curare passed off and the B.P. quickly fell to 80/70. The lungs were inflated with difficulty at this stage. Within five minutes of giving a further 10 mg. tubarine the pressure returned to 140/90. In my opinion this explains many of the reported cases of shock with curare. In other words, to prevent shock one must either produce deep general anæsthesia or adequate curarization. If the operation is nearly finished it is probably more advisable to deepen the anæsthesia so as to obviate the possibility of respiratory depression when the patient has returned to the ward.

(Two charts were shown at the Meeting illustrating the condition of these 2 cases.)

Dr. John Gillies referred to an article by Ranyard West in the *Journal of Physiology*, 91, 437, 1938, in which "The Action of Curarine on the Respiratory Mechanism" was investigated experimentally.

He described the features of a recent personal experience where a patient had died three and a half hours after operation for which *d*-tubocurarine alone was used. The patient, aged 8 weeks, had vomited repeatedly since three days after birth and was in poor condition. At operation no pyloric hypertrophy was found but there were adhesions extending from the second part of the duodenum to the liver and lateral abdominal wall. Separation of the adhesions proved difficult and as kinking of the duodenum still persisted a posterior gastro-enterostomy was performed.

An intravenous injection of *d*-tubocurarine chloride was administered slowly until a total of 5 mg. had been reached. A profound effect of total paralysis of muscles, including the diaphragm, was achieved. It had been intended to keep the child unconscious by means of cyclopropane but this was judged to be unnecessary particularly as there was already an indication of insensitivity when a vein had been cut down upon earlier for the introduction of an intravenous drip.

Throughout the operation which lasted forty-five minutes controlled ventilation of the lungs with oxygen was carried out. Good oxygenation was maintained as evidenced by the colour of the gut. The pulse, visible in the mesenteric vessels, was regular and the rate was steady at 110 per minute. Thirty minutes after closure of the abdomen spontaneous contractions of the diaphragm started but pulmonary exchange being still inadequate the administration of oxygen by compression of the rebreathing bag was continued. On several occasions the mask was removed from the patient's face and a remarkable alteration in pulse-rate occurred. From a rate of 120 the pulse fell to 20 within one minute. On reapplication of the mask and inflation of lung the pulse-rate was restored to 120.

On the third occasion when this sequence of events was demonstrated inflation of the lung was difficult and the heart stopped finally. Post-mortem examination showed collapse of both lungs which presented the appearance of fœtal lungs and did not float.

In the laboratory the clinical events just described were reproduced exactly in a curarized dog, with the exception that the animal recovered completely.

In view of the accidents that have happened during the clinical use of preparations of curare and the post-mortem findings in such cases Dr. Gillies hoped that anæsthetists using this agent would study carefully all the published experimental work.

[*May* 2, 1947]

Controlled Respiration by Means of Special Automatic Machines as Used in Sweden and Denmark. [*Abstract*]

By E. TRIER MOERCH, M.B., B.S., M.D.Copenhagen

MOST operations in the chest cavity can be performed under general, local or spinal anæsthesia without artificial ventilation. However, because of the danger associated with paradoxical respiration, pendulum-air and mediastinal movement, some form of artificial ventilation instead of spontaneous breathing is preferable, at least in major and lengthy intrathoracic operations.

The problem of differential pressure respiration was thoroughly investigated by H. Moelgaard in Copenhagen 1908–1915 and by K. H. Giertz in Stockholm from 1913 to 1916. Giertz showed that artificial ventilation by rhythmic insufflation was superior to the constant differential pressure breathing of the Sauerbruch type.

Starting from Giertz's observations, the Swedish surgeon Frenckner evolved the "Spiropulsator", an air-driven machine, which, during inspiration, fills the patient's lungs with the anæsthetic mixture, and, during expiration, allows the lungs to empty themselves by means of their elasticity, without any resistance.

Since 1933 Frenckner, in collaboration with the Swedish surgeon Crafoord and the engineer Anderson, of the Swedish firm "AGA", has designed for major thoracic operations an anæsthetic apparatus which gives rhythmic ventilation under positive pressure. This "Frenckner-Crafoord-Anderson" apparatus is a combination of the Frenckner Spiropulsator and an "AGA" anæsthetic apparatus built partly on new principles.

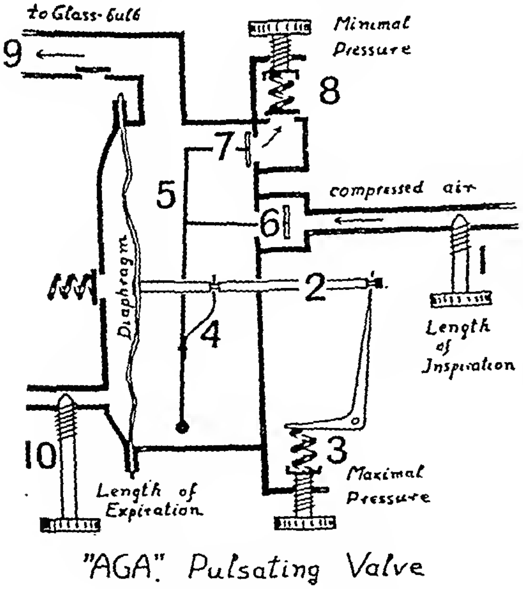


FIG. 1.—The Frenckner "Spiropulsator".

The "Spiropulsator".—Compressed air from an electrically driven air-compressor is led (1) in the main chamber of the valve. As the pressure here increases it presses a diaphragm towards the left (*see* fig. 1). The diaphragm moves a bar (2) towards the left, but the spring (3) tries to move the bar towards the right. As the pressure of air in the valve grows the bar (2) moves towards the left; it presses on the spring (4), the weight-arm (5) moves towards the left and the valve (6) closes while the valve (7) opens. The outlet (9) is connected by a rubber tube to a glass bulb which is airtight and surrounds the breathing bag of the anæsthetic apparatus.

Action of the spiropulsator upon the anæsthetic gases.—When the pressure in the spiropulsator rises, the pressure in the glass bulb rises at the same time, the breathing bag is compressed by the air and the anæsthetic mixture is pressed towards the patient's lungs (inspiration). When the pressure has reached a certain height, which is determined by the position of the screw (3), the diaphragm pulls the arm (5) over

Dr. Halton has done most useful service by emphasizing once again the need for "aided" respiration in all cases which have received tubocurarine. Figures for the incidence of these complications mean little, for so many factors other than the anæsthesia play a part. I am convinced that the use of *d*-tubocurarine by virtue of the light anæsthesia employed must materially reduce post-operative morbidity provided always that the basic physiological facts are borne in mind.

Regarding shock, it has been claimed by some that tubocurarine reduces its incidence, by others that it predisposes to collapse. It is also said that it actually has a protective function; this I do not believe, but the absence of deep anæsthesia enables the patient to recover more quickly from and to compensate better for any circulatory changes which may occur.

Bronchospasm we have never seen. West's work, which is responsible for the fear of this complication, was done with curarine, not tubocurarine, and was performed on dogs. Different species of animals are notoriously variable in their reactions to these substances and until this work has been repeated using pure tubocurarine it would seem of little value.

There is no evidence of increased predisposition to post-operative ileus in these patients. It seems that in a series of over 1,000 chest cases we should have seen one case—in fact we have not.

Finally, I must mention a case to which I have referred where an unforeseen action of tubarine caused the death of a patient.

A patient, aged 40, was bronchoscoped for a suspected carcinoma of the bronchus. The usual technique of anæsthesia was employed and 15 mg. of *d*-tubocurarine (tubarine) was followed by 0·5 gramme of thiopentone. Respiration was abolished and remained absent. He was artificially respirated from the beginning and at no time was there any cyanosis. After half an hour 5 mg. of prostigmin with atropine was given with no result. This was repeated after a further half an hour when a little diaphragmatic movement became apparent, but disappeared after five minutes. The response to further doses given one hour and forty-five minutes and two hours and forty-five minutes after the induction of anæsthesia was similar. After this last dose, however, the diaphragmatic respiration continued, but did not improve in amplitude. All this time his circulatory condition had not shown any change from the satisfactory state in which the procedure was started. Three-quarters of an hour after the last injection of prostigmin he suddenly regurgitated blood-stained abdominal contents in large quantity, some of which entered the bronchial tree. A bronchoscopy was immediately performed and suction instituted. However, the patient's condition deteriorated from this moment and he eventually died five hours and fourteen minutes after the induction of anæsthesia. This case was clearly an exaggerated reaction to a normal dose of tubocurarine—a true idiosyncrasy. That the prolonged respiratory depression was not due to any idiosyncrasy to the barbiturate would seem to be indicated by the fact that there was a small but transient response to the injections of prostigmin. There was no history of any myasthenic symptoms nor was there any thymic tissue found at autopsy. However, there was a very extensive involvement of the left main bronchus by carcinoma. This rendered the whole of the left lung functionless. The right lung showed evidence of the aspiration of a large amount of blood-stained fluid which had undoubtedly reduced the aerating surface of this lung below the minimum required to support life. In the stomach and small intestine there were numerous small punctate hæmorrhages which accounted for the blood-stained stomach contents.

The condition was similar to the hæmorrhages found by Cole (*Anesthesiology*, 1946, 7, 190) in dogs poisoned with a very large dose of intocostrin.

The two main dangers of tubocurarine appear to be its use by the inexperienced and the occurrence of regurgitation of stomach contents. This is an insidious "flow back" of the stomach contents due to the abnormal relaxation of the œsophageal muscle and sphincters.

Dr. Barnett Mallinson, in reply to Dr. G. S. W. Organe: I have not had any venous thromboses with myanesin in my cases so far. As, however, pentothal occasionally causes this complication, if too strong a solution has been used, possibly on occasions thrombosis may have occurred in a vein which had also received pentothal.

In reply to another speaker: An account of post-operative respiratory complications in comparable series of cases with and without curare has been published (Mallinson, *Anæsthesia*, 1946, **1**, 17).

In reply to Dr. Massey Dawkins: As to the value of curare I would suggest that the period of experiment and assessment may occupy a long time yet, but that in time the opposite ends of the pendulum swing will approximate in curare finding its niche. Cyclopropane, after all, remained controversial and experimental for a considerable number of years before taking its present established place.

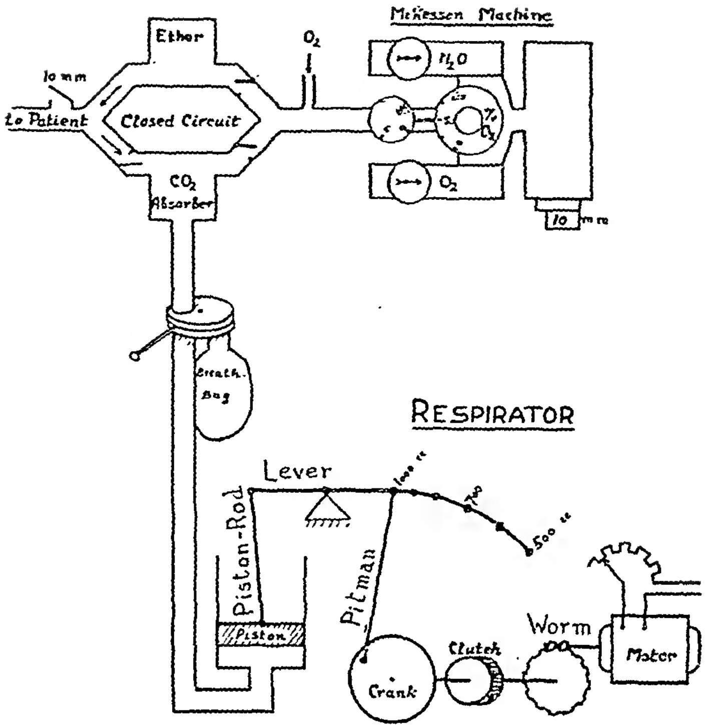

McKesson Machine
Ether
O_2
N_2O
10 mm
To Patient
Closed Circuit
CO_2 Absorber
% O_2
O_2
10 mm
Breath Bag
RESPIRATOR
Lever
1000 cc
750
500 cc
Piston-Rod
Piston
Pitman
Worm
Motor
Clutch
Crank

FIG. 2.—McKesson machine combined with the "Respirator" designed by Trier Moerch.

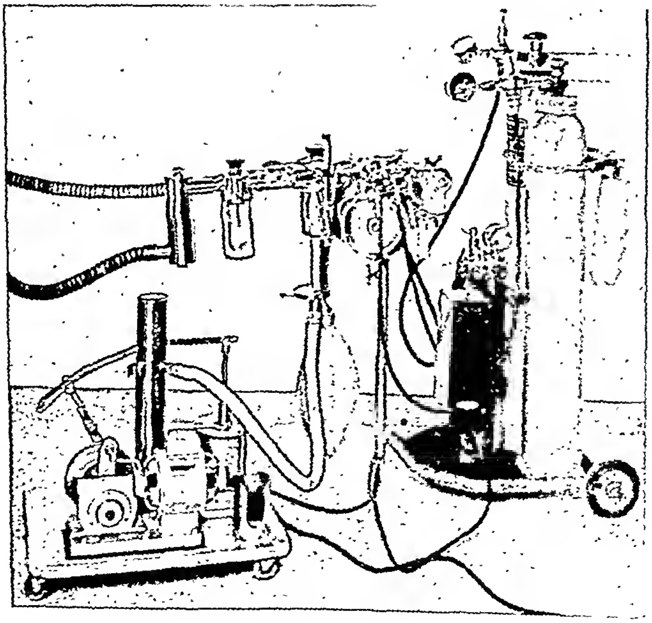


FIG. 3.—McKesson machine with Trier Moerch's "Respirator".

so the valve (6) shuts off the inlet of compressed air and valve (7) opens for the outlet of the air.

The pressure in the pulsator now drops to the minimum pressure determined by the screw (8). The pressure round the breathing bag decreases accordingly and the bag expands because of the recoil of the lungs (expiration). As the pressure on the diaphragm decreases, the spring (3) will pull the bar (2) towards the right, the arm (5) goes to the right, valve (7) closes and valve (6) opens, compressed air streams in again and a new inspiratory phase starts.

By means of the four screws we can alter (*a*) the maximum and (*b*) the minimum pressure, the length of (*c*) inspiration and (*d*) expiration.

The anæsthesia is started in much the same way as in England; a preliminary injection of morphine-scopolamine is given, and local anæsthesia of the throat and larynx is carried out with cocaine or pantocaine. Pentothal or similar preparations (such as evipan, the Swedish barbiturate narcotal, or more often the Danish preparations citodan or narcodorm), nitrous oxide-oxygen and ether or cyclopropane forms the anæsthetic. When the anæsthesia is quiet and some time before the pleural cavity is opened, the spiropulsator is started. After a few minutes, the respiration becomes controlled and is taken over by the machine.

We start the spiropulsator as nearly as possible at the same speed as the patient's spontaneous respiration, but if it is correctly adjusted the spiropulsator automatically finds the rhythm of the patient's respirations. If the patient expires against the spiropulsator, the pressure inside this will rise very quickly and the latter will "click over" to the expiratory phase.

Crafoord has used this machine for several hundred major thoracic operations. In Copenhagen we have used it for about 150 cases.

The "Respirator" designed by the writer.—Having learned the rather complicated method in Stockholm from Crafoord and his anæsthetist (Doctor T. Gordh), I have used it in Copenhagen with excellent results for years. During the war, however, it was almost impossible to import Swedish machines, and as in any case, the machine seemed unnecessarily complicated, I started some experiments in 1940 to adapt the gas-oxygen machines in Denmark (mostly McKesson Nargraf) on similar lines and at the same time to simplify the working principles.

The final machine which I thus evolved contains an electrically driven piston-pump which is inserted into a closed circuit instead of the breathing bag (fig. 2).

An electric motor acts via a worm gearing and a friction clutch on a crank, the pitman of which is connected to one of the arms of a two-armed lever. The other arm of this lever moves via a piston-rod the piston of a single-cylinder pump up and down.

The speed of the pump (i.e. the frequency of the controlled respiration) is regulated by means of a variable electric resistance, mounted in its own box, connected with the anæsthetic apparatus only by a wire (fig. 3), so that one can stand where convenient and watching the frequency of the patient's active respiration adjust the speed of the controlled respiration accordingly.

The clutch is inserted in the slowly moving axle beyond the worm gearing. The friction in the clutch can be conditioned as desired.

The pitman is made of two parts ordinarily in connexion, but which can be disconnected if the supply of electricity should fail (as happened several times during the war) or if something else should happen to the motor. If so, one can continue giving controlled respiration either by working the arm up and down by hand or by the foot or by squeezing the breathing bag by hand.

The pitman is connected to the lever in such a way that the connecting point may be moved along the latter while the machine is working. If the connexion is moved

In the Danish machine the gases are pumped in during inspiration and sucked out during expiration.

Advantages of the automatic machines are the same as of controlled respiration by other means. In addition:

(1) The ventilation can be maintained at a sufficient and fixed level, more accurately than by manually controlled respiration.

(2) The ventilation can easily be changed, little or much, either in frequency and/or depth.

(3) The nerve-impulses from the operation field arise at constant intervals, as in normal respiration: this has presumably a certain importance in diminishing the neurogenic shock from the operation and in maintaining the normal tone of the circulatory medullary centre.

(4) The respiratory part of the circulation, i.e. the venous return of blood to the heart, is supported by the changing pressure inside the thoracic cavity, presumably mostly where positive pressure alternating with suction is applied, as in the Danish machine.

(5) During a thoracotomy when an automatic machine is used, the respiratory movements are very small and take place in an exactly regular rhythm. This is a great help to the surgeon and makes his job easier.

(6) During these extensive and dangerous operations the anæsthetist has much to do. Besides guarding the patient and running the anæsthetic he must watch the transfusion and use his general skill to counteract anything which might disturb the smooth course of the operation. The automatic machines allow the anæsthetist more freedom; he can, without decreasing the ventilation, move from the head of the patient if his help is needed elsewhere in the theatre. He will also have more time for making records.

(7) The ventilation can be recorded exactly, which is of interest both clinically and scientifically.

ACKNOWLEDGMENT

I am indebted to Dr. Crafoord and Dr. Gordh of Stockholm, to the two thoracic surgeons in Copenhagen, Professor E. Husfeldt and the chief surgeon Dr. Tage Kjaer, for all their help; to Dr. phil. O. M. Henriques, the chief of the Finsen laboratory, where the blood estimations were undertaken, and to Major O. Lippmann who has undertaken the technical part of these experiments.

REFERENCES

ANDERSON, EMIL, CRAFOORD, C., and FRENCKNER, P. (1940) *Acta Oto-Laryng., Stockh.*, 28, 95.
CRAFOORD, CLARENCE (1938) *Acta chir. scand.* (Suppl. 54).
FRENCKNER, PAUL (1934) *Acta Oto-Laryng., Stockh.*, 20, (Suppl.), 97.
GIERTZ, K. H. (1916) *Uppsala Läk. Fören. Förh.* (Suppl.) 1-176.
MOELGAARD, HOLGER (1915) Physiological Lung Surgery, Gyldendal (Editor), Copenhagen, 1915 (pp. 1-370).

The full paper will appear in *Anæsthesia.*

Skin Temperature as a Clinical Aid During Anæsthesia. [*Abridged*]

By J. CLUTTON-BROCK, M.B., D.A.

THIS is an account of some purely empirical observations on the use of a skin thermometer during anæsthesia.

I have used a skin thermometer on a great many surgical patients, including most bad risk cases, for rather more than three years and have come to rely more and more on these readings together with those of the blood-pressure, &c., as an indication of the patient's general condition and his need for resuscitative measures.

away from the axis of the lever, the stroke of the piston will decrease until a minimum of 500 c.c. is reached: if the connexion is moved towards the axis, the stroke will increase up to 1,000 c.c.

One-half of the lever is curved. If the lever were wholly straight, the piston would only reach the bottom of the cylinder in one position of the connexion. With the lever bent as a part of a circle concentric with the crank, the piston will reach the bottom of the cylinder whatever the position of the connexion of the pitman (that is, with all stroke-volumes). The dead space will thus be as small as possible.

The cylinder is a simple one without any valves. The pressure of the gases delivered from the pump can be read on a combined pressure and vacuum gauge and varies from about +8 mm.Hg during inspiration to about −3mm.Hg during expiration.

Just above the breathing bag is a mechanism which enables one to disengage the bag from the closed circuit and, instead, engage the respirator.

The whole respirator is built on a little trolley which can be placed a metre or so away from the anæsthetic machine. This distance, plus earthing, ensures against explosion risk.

The anæsthesia is induced as already described. When the respiration is to be controlled, one can either compress the bag until active movements of respiration have ceased and then switch on the respirator, or switch the respirator on straight away. The latter is in fact the easier manœuvre, the motor is started before it is connected to the closed circuit, and the speed adjusted to the speed of the patient's respiration. The clutch is then loosened and the respirator switched into the closed circuit instead of the breathing bag. After the lapse of some minutes, the respirator takes over the respiration of the patient.

If during this time the speed of the respirator does not exactly coincide with the speed of the patient's respirations, the difference is eliminated by the clutch. As a matter of fact it is astonishing how little it matters if there is a difference between these two frequencies. After a short fight the patient gives up and the respirator wins.

Safeguards are already present in the McKesson machine against too-violent action of the respirator, that is either too much suction or too much compression.

The minimum pressure.—If one places the pressure dial on the McKesson machine between "Off" and "O" mm.Hg, the suction will be very little—about 3 to 5 mm.Hg. It can be read on the manometer of the respirator and adjusted on the pressure dial of the McKesson apparatus.

The maximum pressure is limited by the usual McKesson expiratory valve, set to the desired pressure—about 8 to 10 mm.Hg. The McKesson rebreathing bag is opened fully, but the spring is set to say 10 mm.Hg, thus acting as an elastic "buffer" against unexpected sudden changes in pressure.

The McKesson oxygen-percentage-dial is set to a high figure, about 50%, so that if (and when) the respirator sucks from the anæsthetic machine the oxygen content of the gases supplied will be on the safe side.

Apart from these adjustments the McKesson machine with closed circuit is used in the usual way with a continuous supply of basal oxygen, about 300 to 500 c.c. per minute.

Since November 1942 this respirator has been used in 300 cases of major thoracic operations, such as lobectomies, pulmonectomies, ligations of ductus arteriosus, diaphragmatic hernias and transthoracic resections of the upper part of the stomach. The anæsthesias have been quiet, the patients' condition good and the working conditions for the surgeon excellent since the controlled respiration gives such a quiet field.

Differences between the Swedish and the Danish machines.—In the Swedish machine the anæsthetic gases are forced into the patient's lungs during inspiration, but escape during expiration passively by means of the elasticity of the lungs and the thorax.

Section of Endocrinology

President—L. R. Broster, O.B.E., M.Ch.

[*March* 26, 1947]

DISCUSSION ON THE TREATMENT OF TOXIC GOITRE

Mr. J. E. Piercy (*Surgeon i/c Thyroid Clinic*): Primary thyrotoxic goitre offers no difficulty in diagnosis and we find thiouracil invaluable for increasing safety of operation in these patients. It has eliminated the necessity for stage operations in the very severe cases although it increases the technical difficulties.

We feel that the secondary nodular thyrotoxic goitre which leads insidiously to cardiac damage culminating in paroxysmal or established auricular fibrillation is the type which most needs recognition, particularly the apparently non-toxic nodular gland with few symptoms other than tiredness, irritability and occasional palpitation, often with a basal metabolic rate within normal limits.

There is a very great difference clinically between primary and secondary toxic goitre, and I have yet to find a patient with a nodular goitre giving a history suggestive of primary Graves' disease earlier in life. The importance of this must be appreciated when we find that 22% of 1,000 patients with nodular goitres had developed auricular fibrillation by the time they were sent for operation—40% between the ages of 50 and 60, and 30% between 40 and 50. Of these 220 patients 78% were discharged with normal rhythm after operation, either occurring spontaneously, or after a short course of quinidine. They do not include the many patients with minimal thyrotoxicosis, some showing signs of pressure symptoms only, who developed a transient post-operative fibrillation. These were at the point of developing paroxysmal or established fibrillation before operation and this should not be looked upon as a complication of the operation but as evidence that they were at a late stage in the disease.

Our procedure is one of close collaboration between physician and surgeon and carefully organized team-work. The pre- and post-operative procedure depends solely on the individual merits of each case. There can be no uniformity in regard to the pre-operative period of rest and iodine or in the type of operation performed.

We feel that ligation of the inferior thyroid arteries lessens the possibility of recurrence because we have had none to our knowledge in 550 patients treated in the past seven years, whereas in the previous seven years 750 operations were performed and the vessels were not ligated and 6% of these patients had recurrences. A recurrence in secondary toxic goitre is often due to the fact that the opposite lobe was not explored and to its being really a case of continued growth in the unexplored lobe.

In the ordinary way when we assess a patient's condition, we include rough estimates of the state of his peripheral circulation. We feel the temperature of his skin and note his colour. It has been shown that temperatures within a range of 5° C. above or below that of the examining finger will not be appreciated as either warm or cold [1]. Variations in the skin temperature, however, give a reasonably accurate idea of any changes in the state of the peripheral circulation.

The technique is simple, a mercury in glass thermometer is used. This is made without a constriction and reads from 80° to 107° F. The bulb is in ring form and partly enclosed in a reflecting hemispherical case, making with the patient's skin a reasonably airtight fit, thus avoiding changes in the readings due to draughts, &c.

The thermometer is attached by elastoplast to the patient's forehead. This position is chosen because the skin of the forehead shows least response to environmental changes of temperature [2].

There is considerable individual variation in the skin temperature of the face in normal patients [2], so, within limits, changes in temperature rather than absolute readings are considered to be of significance.

The constriction of the vessels of the skin is one of the compensating factors in shock, and I think a measurement of this vasoconstriction is, to a close approximation, a measurement of the degree of shock present.

The skin temperature of the patient's face usually rises with the induction of any anæsthetic, the absence of this vasodilatation apparently having a grave prognostic significance [3]. After this initial rise, it will remain steady unless shock occurs when it may fall. A fall of 1° F. or less is of minor significance, but 3° or more shows, I think, a considerable degree of shock.

The variation in skin temperature bears very little relation to that of the blood-pressure. A very considerable fall in blood-pressure may occur without a fall in skin temperature, the fall in blood-pressure being due perhaps to a high spinal, large quantities of local anæsthetic solution, changes in position of the patient, changes in the percentage of the anæsthetic gases, or any other cause producing sluggishness of the circulation without true shock. In one case the patient's blood-pressure fell to 40 mm. systolic and 20 mm. diastolic after a high spinal for a combined synchronous excision of the rectum. The blood-pressure remained at this level for more than one hour.

Provided that there has been no fall in skin temperature, I have never found any harm come to a patient whatever his blood-pressure. When, however, the blood-pressure and skin temperature have fallen together, the patient has been critically ill and needed energetic resuscitation.

In some cases a sustained blood-pressure, or even a rise, has been seen with a fall in skin temperature. This is not uncommon, presumably the vasoconstriction which causes the fall in skin temperature also sustains the blood-pressure. The patient in these cases has been shocked but has compensated well for his shock; however, it is important to realize that the condition of shock is present and that the patient requires careful watching.

By taking skin temperatures we can distinguish between falls in blood-pressure due to shock and falls due to other causes of little significance. With skin temperature and blood-pressure readings together the patient's need for resuscitation can be better judged.

REFERENCES

1 TROTTER, W., and DAVIES, H. M. (1909) *J. Physiol.*, 38, 134.
2 BENEDICT, F. G., and PARMENTER, H. S. (1928) *Amer. J. Physiol.*, 87, 633.
3 IPSEN, J. (1929) *Acta chir. scand.*, 65, 226.

The full paper will appear in *Anæsthesia.*

Section of Endocrinology

President—L. R. Broster, O.B.E., M.Ch.

[*March* 26, 1947]

DISCUSSION ON THE TREATMENT OF TOXIC GOITRE

Mr. J. E. Piercy (*Surgeon i/c Thyroid Clinic*): Primary thyrotoxic goitre offers no difficulty in diagnosis and we find thiouracil invaluable for increasing safety of operation in these patients. It has eliminated the necessity for stage operations in the very severe cases although it increases the technical difficulties.

We feel that the secondary nodular thyrotoxic goitre which leads insidiously to cardiac damage culminating in paroxysmal or established auricular fibrillation is the type which most needs recognition, particularly the apparently non-toxic nodular gland with few symptoms other than tiredness, irritability and occasional palpitation, often with a basal metabolic rate within normal limits.

There is a very great difference clinically between primary and secondary toxic goitre, and I have yet to find a patient with a nodular goitre giving a history suggestive of primary Graves' disease earlier in life. The importance of this must be appreciated when we find that 22% of 1,000 patients with nodular goitres had developed auricular fibrillation by the time they were sent for operation—40% between the ages of 50 and 60, and 30% between 40 and 50. Of these 220 patients 78% were discharged with normal rhythm after operation, either occurring spontaneously, or after a short course of quinidine. They do not include the many patients with minimal thyrotoxicosis, some showing signs of pressure symptoms only, who developed a transient post-operative fibrillation. These were at the point of developing paroxysmal or established fibrillation before operation and this should not be looked upon as a complication of the operation but as evidence that they were at a late stage in the disease.

Our procedure is one of close collaboration between physician and surgeon and carefully organized team-work. The pre- and post-operative procedure depends solely on the individual merits of each case. There can be no uniformity in regard to the pre-operative period of rest and iodine or in the type of operation performed.

We feel that ligation of the inferior thyroid arteries lessens the possibility of recurrence because we have had none to our knowledge in 550 patients treated in the past seven years, whereas in the previous seven years 750 operations were performed and the vessels were not ligated and 6% of these patients had recurrences. A recurrence in secondary toxic goitre is often due to the fact that the opposite lobe was not explored and to its being really a case of continued growth in the unexplored lobe.

Our mortality at the Thyroid Clinic on thyrotoxic goitres is 1·3% since 1932, but in recent years it has been a fraction of 1%. I have personally had three deaths in my last 500 cases, two of them from pulmonary embolism occurring on the ninth and tenth days.

No patient however toxic and emaciated or whatever the severity of cardiac damage is considered inoperable but we feel that perhaps the ones needing most consideration are those with an associated mental derangement.

Complications.—No thyrotoxic crisis has been seen for some years. Symptoms due to injury of the recurrent laryngeal nerve occurred in 21, or nearly 2% and all but one of these was of a transient nature. In the one persistent case the symptoms began three weeks after operation. Thirteen patients developed tetany, generally of a transient nature which quickly responded to intensive calcium therapy. In only three was parathyroid extract necessary and they ultimately became symptom-free. Two patients who developed myxœdema still require thyroid treatment but others of a mild degree have later recovered their metabolic balance by regeneration of the remaining thyroid tissue.

Results.—In the average patient a return to normal or near normal health can be expected, whilst a large measure of recovery can be anticipated even in severely toxic patients and in those with complications. Thyrotoxicosis commonly occurs in the highly-strung, sensitive type of person and though thyroid balance may be regained by operation, the constitutional make-up is not altered. It is generally recognized, however, that the nursing profession is an exceptionally arduous and exacting one and the fact that of 67 nurses who underwent partial thyroidectomy all returned to full duty is an indication of the effectiveness of the operation.

We have not used thiouracil at our clinic as treatment so I cannot pretend to have any experience of it as such. I am, perhaps, biased therefore as my only experience of the drug, apart from pre-operative and diagnostic use, is from those many cases of thiouracil failure and intolerance, sent to us for operation from hospitals both in London and in the Provinces. These patients were many and varied, males and females with primary and nodular goitres, some having had the drug for as little as three weeks and some up to two years. The majority had improved but treatment had been stopped for various reasons, including leucopenia, nausea and vomiting, thrombocytopenia, attacks of tetany, œdema of legs with urticaria, increasing size of gland and vomiting, leucopenia with præcordial pain, recurrence of symptoms while under treatment, lack of response to thiouracil, continued auricular fibrillation with evidence of heart failure, and failure to co-operate with the physician.

All of these patients had been treated in hospitals under medical supervision, one of them for as long as one and three-quarter years, and I am certain that every effort had been made for a successful trial before the patients were sent to us for operation.

In surgery, not only is the thyrotoxicosis dealt with rapidly, once and for all, but also the goitre, which is liable to cause pressure symptoms, to be subject to hæmorrhage, occasionally to become malignant, and even by its mere presence to cause endless worry and anxiety. Moreover, the risk of future auricular fibrillation is practically removed.

To my mind surgery offers a more certain and more rapid cure than does thiouracil and the mortality is no greater.

Dr. W. R. Trotter: *The treatment of toxic goitre by thiouracil.*—In the experimental animal the primary effect of administering thiouracil is that the production of thyroid hormone ceases. As a consequence the metabolic rate falls and signs of myxœdema eventually appear. What has been achieved is, in effect, a pharmacological thyroidectomy, differing only from the surgical operation in that its effects may be reversed by discontinuing the drug at any stage in its administration.

A secondary result of the administration of thiouracil to an experimental animal is hyperplasia and hypertrophy of the thyroid gland. This is believed to be due to an excessive secretion of the thyrotropic hormone of the pituitary, provoked by the low level of circulatory thyroid hormone.

Physiological experiment therefore leads us to expect that if this drug is given to a patient with a toxic goitre it will be possible to reduce or abolish the manifestations of thyrotoxicosis. But since there is no evidence that thiouracil has any permanent effect on the thyroid it is to be expected that if the drug is discontinued the symptoms will immediately recur, unless by that time a natural remission of the disease has taken place. We shall certainly not expect any reduction in the size of the goitre and shall not be surprised to find that it becomes larger. We shall also not expect any amelioration of exophthalmos or ophthalmoplegia, since there is reason to believe that they are not the result of thyrotoxicosis as such.

It is obvious that the practical utility of the drug will depend, first, on its ability to control the symptoms of thyrotoxicosis; secondly, on its toxicity; and, thirdly, on the frequency with which natural remission occurs. If thiouracil is to supplant surgery as the standard treatment of toxic goitre it must be shown that it can control thyrotoxicosis as effectively as thyroidectomy and that it is no more dangerous than the operation. If these postulates can be fulfilled then thiouracil is clearly a useful method of tiding a patient over a relatively brief phase of thyrotoxicosis, but it would still not be a very acceptable form of therapy if it had to be continued for a lifetime. Most patients would probably prefer to swallow pills for a limited period rather than undergo a major operation; but they would probably prefer the operation to the prospect of remaining under close medical supervision for the rest of their lives. Much therefore depends on the natural course of the disease.

For the most part the theoretical forecasts have been confirmed by clinical experience. The only major exception has been the enlargement of the goitre which might be expected to occur regularly during thiouracil treatment but which in fact appeared in only 8% of our cases. Usually, but not invariably, when the goitre enlarges symptoms of myxœdema also appear. Lowering the dose of thiouracil abolishes the signs of myxœdema, and the gland reverts to its previous size. It seems that in order to cause enlargement of the goitre one has to give a dose greater than that which is necessary to control the thyrotoxicosis. In other words, when enlargement of a goitre occurs during thiouracil treatment it is simply an indication of overdosage.

The control of thyrotoxicosis by thiouracil which is theoretically to be expected obtains also in practice. The short-term effects of this drug are too well known to need further description. Only in cases which have had much iodine do we fail to get a well-marked response within a few weeks of the start of treatment. However, iodine can also produce a prompt response when given to a thyrotoxic patient for the first time, and it is clearly necessary to show that the control exercised by thiouracil can be maintained for long periods. Some results recently published by Professor Himsworth, Dr. Morgans and myself (1947, *Lancet* (i), 241) seem to suggest that this is in fact the case. Two series of patients were compared over a period of thirty months: 93 were treated by subtotal thyroidectomy, and 65 with thiouracil. The latter were treated initially in hospital with thiouracil or methyl thiouracil in a dosage of 600 mg. daily. They then continued as out-patients on 100 mg. daily. This was later reduced to 50 mg. daily or 50 mg. on alternate days, according to their progress. The method of assessment of results was to find out what proportion, in each series, could be considered "apparently cured" at different stages up to thirty months. This term means that the patients were free of all thyrotoxic symptoms and had pulse-rates of 80 or less. It will be seen that about one-third of the cases in both series attained this standard throughout the period of observation. The remainder either had slight symptoms, such as occasional palpitations, or their pulse-rates were a little over 80. In both series all patients obtained considerable benefit from their treatment and had resumed their normal occupations. It was also found that the average weight curves of the two series ran closely parallel. We concluded from these observations that thiouracil maintains its control for periods of up to thirty months, and that that control is of the same order of efficacy as that produced by thyroidectomy.

We have been able to study 29 patients who have been kept under observation for six months or more since thiouracil was stopped (fig. 1). When more time has elapsed we are clearly going to get valuable information from studies of this type about the natural course of the disease. Although the numbers are few and the time of observation short there are already some points of interest to be observed. The duration of the course of thiouracil varied from four to thirty-two months, the average being sixteen months. In 7 patients symptoms recurred after intervals of five to twenty-nine months from the time of stopping treatment (average fourteen months). Since the symptoms did not return immediately it seems likely that these were true recurrences of the disease, and not merely the result of stopping treatment too soon. Our policy is to continue treatment until the patient has remained symptomless on the minimum dose (50 mg. on alternate days) for at least three months, and this seems to be a safeguard against too early cessation of treatment. It may be remarked that in some other published series, in which high relapse-rates are reported, the majority of relapses have occurred within one or two months of the end of treatment, which clearly had been terminated too soon.

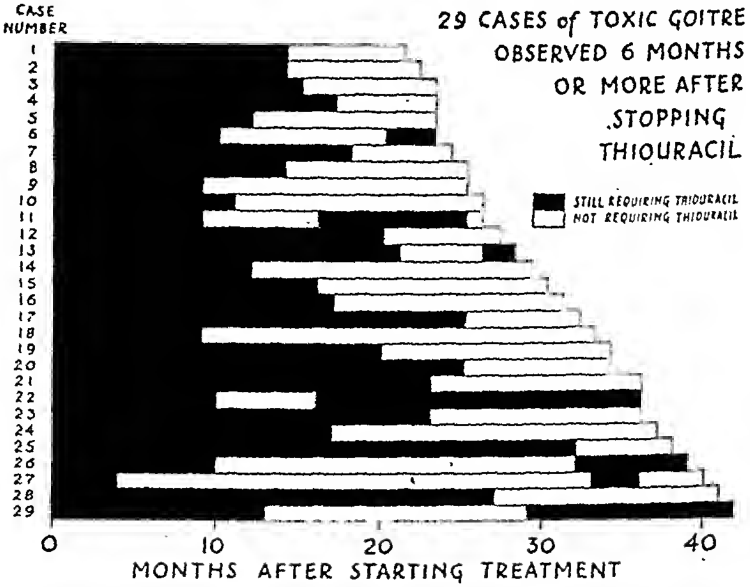


Fig. 1.

Our experience shows that in some cases a natural remission can be expected to set in within a year or two of the patient first coming under treatment. How durable this remission will be remains to be seen. From the obvious well-being of some of these patients at periods of a year or more after the end of treatment, and from the way in which their goitres have shrunk, one may well expect that in some at least the remission will be permanent. There is therefore reason to believe that in a proportion of patients with toxic goitre the disease becomes extinct within a year or two. Such patients need to have their thyrotoxicosis kept under control for this relatively short period, and the administration of thiouracil is a simple and satisfactory way of exercising this control. What we need now is some way of distinguishing this type of case from those whose disease persists for many years or who show a continued tendency to recur.

We think therefore that thiouracil is capable of controlling thyrotoxicosis and that the disease is one in which natural remission occurs often enough for a remedy of this kind to have its uses.

The common complications of thiouracil therapy are skin rashes, drug fever and leucopenia. However, these conditions do not amount to much more than a nuisance and at their worst may lead to discontinuance of thiouracil. Agranulocytosis is a very different matter. Its high death-rate and unexpected onset make it one of the most alarming conditions to be encountered in medicine. It is the cause of all the recorded deaths from thiouracil. There is at present no known way of preventing agranulocytosis, but alertness and promptitude in diagnosis and treatment will do much to prevent it being fatal. It is very necessary that patients on thiouracil should be warned to report at once if they develop fever or a sore throat and that they should immediately discontinue the drug. In such an event a blood-count must be done immediately and if no polymorphs are present penicillin should be started at once. If a patient with agranulocytosis can be protected from infection during the critical period he will probably survive.

But although agranulocytosis is alarming it is fortunately rare. The large series of cases, amounting to several thousands, collected by Moore, F. D. (1946, *J. Amer. med. Ass.*, **130**, 315), and by van Winkle and others (1946, *J. Amer. med. Ass.*, **130**, 343), show that the death-rate due to thiouracil amounts to about 0·5% of all cases treated. These figures include the early cases when agranulocytosis was not anticipated, and not all the patients with agranulocytosis were treated with penicillin. The present day mortality-rate is therefore probably less. Hence it may be said that the mortality-rate of thiouracil is at least as small as that of thyroidectomy in the hands of an expert surgeon.

In summary, thiouracil can be said to be a safe and effective method of keeping thyrotoxicosis under control. It has no curative action and therefore is only useful in cases in which the disease is not likely to last an inordinately long time. So far as our early experience goes it looks as if a fairly large proportion of cases of toxic goitre will be found to fall into this class.

If this new agent is to be compared with the well-established method of subtotal thyroidectomy it is clear that the comparison must depend on two circumstances: first, the type of surgery with which it is to be compared, and secondly the type of case which is being treated.

Subtotal thyroidectomy can be a very difficult operation. The safety with which it can be performed depends not only on the skill of the surgeon and his team, but also on his familiarity with the operation. By the time a surgeon has done several hundred thyroidectomies we can safely assume that his mortality-rate has fallen to the region of 1% or less. Most general surgeons do not acquire this degree of experience and their mortality is correspondingly higher than that of their colleagues who have made a special study of the operation. It follows that thyroidectomy in the hands of an expert is about as safe as treatment with thiouracil, but that thyroidectomy by surgeons without much experience of the operation is less safe than thiouracil—in some cases much less safe. In places where specialized surgery is not available, therefore, a physician may be well advised to treat all his cases with thiouracil, in the expectation that by so doing he will be saving lives.

When expert surgery is available we can afford to exercise more discrimination. Here surely the aim should be to learn to distinguish the short-term from the long-term cases. By the long-term cases I mean those patients whose thyrotoxicosis seems likely to last many years and for whom thyroidectomy would be a more appropriate remedy. We have, for example, under our care a man of 57, whose thyrotoxicosis began first in 1917. A partial thyroidectomy was performed and he remained well until 1933 when the symptoms returned. He has now been under treatment with thiouracil continuously for two years. So long as the dose is maintained at 100 mg. daily he remains well, but thyrotoxic symptoms have appeared on the three occasions when it has been decreased below this level. It now seems as if he will need thiouracil for many years—perhaps indefinitely. This is a case in which a further thyroidectomy might have been a more appropriate treatment.

In toxic nodular goitre, too, we are dealing with a condition in which natural remission is unlikely, for the symptoms seem to be related as much to the patient's age and cardiac state as to the state of the goitre itself. In these patients an element of mechanical obstruction is very common and there are therefore double grounds for supposing that they are best dealt with by thyroidectomy.

As a contrast I will quote the case of a woman aged 42, who started treatment in April 1944. Initially she had an easily palpable diffuse goitre and unilateral lid retraction. The initial sleeping pulse-rate was 110, and the B.M.R. + 53%. She made a good response in the first month of treatment and was afterwards maintained free of symptoms on 50 mg. daily, and then on 50 mg. on alternate days. Thiouracil was stopped after treatment had continued for nine months in all. She has been observed for a further two years since then. She says she has never felt so well in her life. Her goitre is no longer visible and scarcely palpable; and the lid retraction has gone. She has gained 2½ stones in weight, and her pulse-rate at the last six attendances has varied between 68 and 80. It seems to me that thiouracil in such cases is the best form of therapy.

Dr. A. M. Nussey: My remarks are based on experience in 75 cases treated with thiouracil in the course of three and a half years. I would like to emphasize that anyone attempting to treat cases of thyrotoxicosis with thiouracil should follow them right through, for years, if need be.

After a preliminary B.M.R., white cell and polymorph counts, every patient is given the choice of surgery or medicine and, if thiouracil is preferred, is warned of the possible dangers. I used to admit patients for at least a week, and longer if such complications as congestive heart failure and auricular fibrillation were present, but now practically all, with exception of the so-called thyro-cardiacs, are treated as out-patients, and those who are gainfully employed are allowed to go on working while the treatment is progressing. They are seen at weekly intervals twice or three times, then every other week, then every third week and finally, while the treatment lasts, not less than once in every four weeks. At such a visit the patients are assessed in a general way, white cell and polymorph counts are done, the neck measured and weight recorded. In the light of experience I now treat all patients for not less than eight months, even if they respond very rapidly. After treatment stops they are followed up every two months and then once every three months, and with few exceptions, their co-operation has been very good. At present I have thirty patients, half of whom had severe or very severe symptoms and the other half moderate or mild, who had remissions for not less than five months after periods of treatment varying from three to fifteen months, the average being about seven months. Four of those had relapses which necessitated more than one course. Ten have been free of symptoms for longer than two years, the longest being two years nine months, and eleven for more than a year. On the other hand one of my first patients has had to have thiouracil with short remissions for over three years. Relapses, which are often preceded by emotional stress, do, as a rule, respond to further courses of treatment.

Dosage.—I generally start with 0·1 gramme of methyl thiouracil q.i.d. and after two, three or four weeks reduce it to 0·1 gramme t.i.d. Then further reductions are made to 0·05 gramme q.i.d., t.i.d., and b.d. and quite a number of my patients are maintained on 0·05 gramme daily.

With thiouracil the thyroid gland softens slightly, and only rarely does it become smaller. In many patients there is a slight enlargement, and in some of the early ones, where we used larger doses than we are accustomed to do now, the neck swelled up considerably, though the process was found to be reversible when the dose of the drug was reduced. The neck measurements already mentioned serve as a rough guide, but of course some of the increase in circumference is often due to the quite appreciable gain in weight observed in most cases.

I have not found exophthalmos much affected by the treatment, but in one patient unilateral exophthalmos regressed completely with thiouracil. Seven patients had auricular fibrillation and the rhythm returned to normal in four, one with the aid of quinidine, but in the three others there has been no change. Two patients conceived in the remission stage (one of those had had a stillbirth before thiouracil treatment) and both had healthy children. Another was treated for five months ending six weeks before term and she was delivered of a normal baby.

Complications of a minor type like fleeting macular rashes, enlargement of salivary glands and a tendency to leucopenia were met in about 10% of the patients, but hardly at all in the last twenty. It is fair to point out that with such prolonged treatment all kinds of symptoms may arise, and some may be unjustly blamed on thiouracil. Two serious complications occurred, one in a woman of 59 who developed almost complete agranulocytosis and who eventually responded to intravenous pyridoxine, and another in a female diabetic of 65 who had an intense maculo-papular rash, splenomegaly and fever, without a drop in the white cell count.

Two patients were operated on because thiouracil failed to control the disease fully but in both, after an extensive ablation of the thyroid, further treatment with thiouracil was required. A third was operated on at the patient's request after she suffered a relapse and a fourth is awaiting operation because of her lack of co-operation.

The usual contra-indications to the use of thiouracil are:

(1) Where the patient, for cosmetic or other reasons, expresses a preference for surgery; (2) where the gland exerts pressure; (3) where, in the course of treatment, serious complications arise, such as agranulocytosis and recurring rashes with fever; (4) where the disease cannot be controlled without pushing the drug to dangerous limits; (5) where co-operation by the patient is lacking.

At present I would suggest three years as an arbitrary period for length of treatment, after which only the patient's express wish to avoid surgery would justify further use of thiouracil.

Mr. R. Vaughan Hudson: Thiouracil is a sign-post on the road to medical treatment but is not the complete answer to our problems. It is essential that the effects of thiouracil be fully investigated, and the indication for its use and the knowledge of its limitations made known. On the other hand the random use of thiouracil must be deprecated. The patient should be warned of its uncertainties and of its dangers, and treatment only undertaken by competent physicians, with a knowledge of the vagaries of thyrotoxicosis, who will undertake a full investigation of their patients, and keep them under supervision for a number of years.

Failures of prolonged thiouracil treatment which eventually come to operation render the surgical technical problem much more difficult. Mortality and morbidity in these cases should be credited to the results of medicine rather than be attributed entirely to surgery.

Although a division of the cases into primary and secondary thyrotoxicosis is useful I do not consider that there is any essential difference between the two. For instance in 150 personal cases of arrhythmia, we found that the arrhythmia was due to primary thyrotoxicosis more commonly than to secondary thyrotoxicosis and nodular goitre.

Dr. A. C. Crooke: Improvement in the results of medical treatment of toxic goitre may be anticipated and it is unfair to compare the present results of thiouracil therapy, which is still in its infancy, with surgery, which has, perhaps, reached the peak of its perfection. Rather the results of thiouracil therapy to-day should be compared with surgery in its infancy, when it will be realized how valuable a drug we have to deal with.

New advances are being made and in 1943 Astwood, Bissell and Hughes had reported on the comparison of 220 compounds with thiouracil, 115 of these had detectable antithyroid activity and 15 were more potent than thiouracil. The most active of them were 6-n propyl thiouracil, which was eleven times, and 6-n benzyl thiouracil, which was ten times as active as thiouracil. In 1946 Astwood and Van der Laan reported on the treatment of 100 unselected patients with propyl thiouracil, none of whom had any toxic reactions. If this work is confirmed by others, then we have in propyl thiouracil a drug which is as simple, as safe and as effective for the treatment of thyrotoxicosis as thyroid extract is for the treatment of thyroid insufficiency.

REFERENCES

ASTWOOD, E. B., BISSELL, A., and HUGHES, A. M. (1945) *Endocrinology*, 37, 456-481.
——, and VAN DER LAAN, W. P. (1946) *Ann. intern. Med.*, 25, 813-821.

Section of Medicine

President—MAURICE DAVIDSON, M.D.

[*February* 25, 1947]

DISCUSSION: TREATMENT OF THE LYMPHADENOPATHIES

Dr. R. Bodley Scott: *Treatment of the primary lymphadenopathies.*—By the ungainly title of primary lymphadenopathy is meant all those disorders which manifest themselves first by enlargement of lymph nodes. Those which particularly call for discussion are the proliferative and neoplastic diseases of lympho-reticular tissue, or what are now often called the reticuloses and the reticulosarcomata. Of the former the commonest examples are Hodgkin's disease, lymphatic leukæmia, lymphoid follicular reticulosis (follicular lymphoblastoma of Brill and Symmers), and lympho-reticular reticulosis (Hodgkin's paragranuloma); of the latter, the lymphoblastic reticulosarcoma (lymphosarcoma).

The therapeutic problems raised by these disorders are numerous, and at the present time unsolved because the cause of none of them is known, and the very nature of the reticuloses is matter for debate. I believe it to be important that the general direction of treatment of these disorders should rest with a physician and not with the practitioner of some specialized form of therapy.

It may be stated at the outset that, as the cause of these diseases is unknown, there is for them no curative, or even logical, treatment. Trousseau's comment that a diagnosis of Hodgkin's disease is a sentence of death is as depressingly true now as it was in 1866, and can be extended to most of the other diseases under consideration.

The long tale of discarded remedies indicates a sorry record of therapeutic failure, and in Hodgkin's disease particularly a number of methods of treatment have been used which have now only a historical interest. These are, in the main, measures which assumed that the disease had an infective origin: vaccines prepared from the diphtheroids isolated from lymphadenomatous tissue by Bunting and Yates; immune sera against these bacteria, and against emulsions of diseased lymph nodes; sensitized vaccines of supposed virus bodies obtained from such emulsions; homologous serum from other patients with Hodgkin's disease; extracts of spleen; suprarenal extracts;

and Coley's fluid. The demi-monde of immunotherapy has been fully explored and its products found ineffective. Likewise the pharmacopœia has been ransacked: quinine, trypan blue, benzol, iodine—in organic and inorganic combination, cerium, manganese, gold, iron, bismuth, mercury, and antimony have all been recommended and duly discarded.

At the present time our ignorance of their causation forces us to apply the same general principles of treatment to the many different histological types of reticulosis and reticulosarcoma. The two therapeutic aims commonly pursued are to destroy the pathological tissue and to preserve the patient's general health.

It is assumed that the patient will benefit if the enlarged lymph nodes can be induced to shrink to normal size and the pathological cells in them destroyed. To effect this the destructive agent commonly used is X-radiation. There is little evidence, however, that life is prolonged by such measures. It is difficult to obtain satisfactory statistics for these diseases because the histological criteria for diagnosis are not yet agreed, and because no untreated control series is available. In respect of Hodgkin's disease, however, the series of Baker and Mann (1939) is comparable with that of Desjardin and Ford (1923); in the former radiotherapy was adequate, in the latter the authors state that many cases had no radiotherapy and in none was it satisfactory, even by the standards of twenty-three years ago. The graph of survival (fig. 1) in the two series shows no appreciable difference until the percentages for those living after five years are reached when the figures are 19% and 7·9%; however, this difference is not significant, its standard error being 5·8. There is, therefore, little reason to suppose that radiotherapy, judged to be "adequate", prolongs life in Hodgkin's disease. For other types of reticulosis and for reticulosarcoma similar figures are not available, but there is no reason to suppose that they would show any striking difference.

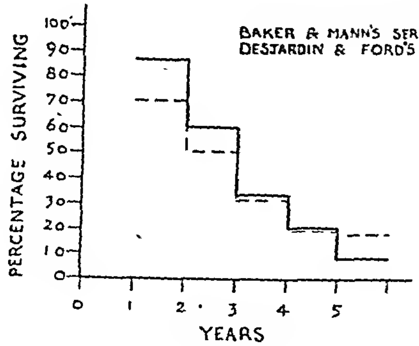


FIG. 1.—Percentage of patients with Hodgkin's disease surviving at the end of yearly periods.

No one would deny that radiotherapy is often followed by improvement in all these disorders, but this is transitory. Enlarged nodes disappear, fever vanishes, pruritus is controlled, and the patient's general health, for a time, shows great benefit.

From the point of view of treatment it is convenient to divide reticulosis and reticulosarcoma into two broad groups, depending on whether the disease is localized to one or two contiguous groups of lymph nodes, or is virtually systematized throughout the lympho-reticular tissue. Into the first category fall Hodgkin's disease, lympho-reticular, and many of the less common reticuloses and reticulosarcomata; into the second, lymphatic leukæmia, lymphoid follicular reticulosis, and lymphoblastic reticulosarcoma. This division, is, of course, not absolute and variations occur in both directions, but it is true to say that the majority of the first group start as localized disorders, while the majority of the second are generalized *ab initio*. It is clear that this peculiarity has important bearings on treatment: in the former irradiation of one group of nodes is all that is required, in the latter the whole body may demand treatment.

In the first group radiotherapy yields results which are temporarily satisfactory, and, with possible exceptions which I will discuss later, it is at present the treatment of choice. The situation in the second group is different: the patient may have no symptoms arising from the nodal enlargements which are often discovered by chance. This is especially true of chronic lymphatic leukæmia in the elderly, a disorder which is often revealed by a blood-count done for some other reason; the lymph-node enlargement being found only when the blood-count invites a search. In the latter half of life this disease is often virtually benign; it may run a course of ten or twelve years. I have recently seen a patient who has remained in good health without treatment for nine years. Radiotherapy can control some symptoms, there is no evidence that it prolongs life, and it is irrational to prescribe it until symptoms exist. No patient is distressed because his blood contains more than the usual number of lymphocytes, and however much satisfaction the physician may derive from restoring the count to normal there is no reason to suppose the patient benefits from the alteration. In this type of case irradiation should be withheld until local masses cause pain or disfigurement or until anæmia demands intervention. In lymphoid follicular reticulosis again the place of radiotherapy is less certain than it formerly seemed; many of these cases terminate by sarcomatous change, but the disease progresses slowly until this occurs. It is the impression of many clinicians that irradiation may accelerate this metamorphosis. Thus if irradiation is employed, caution is advisable and it seems wise to defer it until symptoms become insistent. In lymphoblastic reticulosarcoma the course is rapid, radiotherapy usually has to be applied by the "bath" method, and the remissions it produces are short-lived and few; nevertheless it is, at present, the best method available of palliating the patient's discomforts.

Surgery in the treatment of these diseases has been decried in the past, but Baker and Mann in 1939 noted that two cases in their series had continued without recurrence ten and twelve years respectively after total extirpation of the affected lymph nodes. This procedure is clearly applicable only to those in whom one superficial group of nodes is diseased, that is to certain of the first category. Suitable cases are rare for in 80% of the common cervical type of Hodgkin's disease there is radiological evidence when the patient is first seen of enlarged mediastinal nodes. I have seen complete freedom from recurrence for four and eight years after surgical excision of the affected nodes, the first in Hodgkin's disease and the second in lympho-reticular reticulosis. In such cases I now recommend surgery but it will be some time before its exact value and indications can be appraised.

Chemotherapeutic attempts to reduce the size of the enlarged nodes began with Billroth's introduction of arsenic in 1871. It has been used consistently since then, in organic and inorganic forms. Its value is hard to assess. The older clinicians were loud in its praises, but it is sometimes difficult to avoid the iconoclastic suspicion that they were easily pleased. Arsenic, seldom, if ever, diminishes the size of the lymph nodes, but it is often reported to have a beneficial effect on the patient's general health.

Recently interest has been aroused by reports from the United States of the use of compounds of the nitrogen mustard series in these disorders. The substance most extensively employed has been methyl-bis (beta-chloroethyl) amine hydrochloride. It is given intravenously in doses of 0·1 mg. per kg. body-weight daily for four con-

and Coley's fluid. The demi-monde of immunotherapy has been fully explored and its products found ineffective. Likewise the pharmacopœia has been ransacked: quinine, trypan blue, benzol, iodine—in organic and inorganic combination, cerium, manganese, gold, iron, bismuth, mercury, and antimony have all been recommended and duly discarded.

At the present time our ignorance of their causation forces us to apply the same general principles of treatment to the many different histological types of reticulosis and reticulosarcoma. The two therapeutic aims commonly pursued are to destroy the pathological tissue and to preserve the patient's general health.

It is assumed that the patient will benefit if the enlarged lymph nodes can be induced to shrink to normal size and the pathological cells in them destroyed. To effect this the destructive agent commonly used is X-radiation. There is little evidence, however, that life is prolonged by such measures. It is difficult to obtain satisfactory statistics for these diseases because the histological criteria for diagnosis are not yet agreed, and because no untreated control series is available. In respect of Hodgkin's disease, however, the series of Baker and Mann (1939) is comparable with that of Desjardin and Ford (1923); in the former radiotherapy was adequate, in the latter the authors state that many cases had no radiotherapy and in none was it satisfactory, even by the standards of twenty-three years ago. The graph of survival (fig. 1) in the two series shows no appreciable difference until the percentages for those living after five years are reached when the figures are 19% and 7·9%; however, this difference is not significant, its standard error being 5·8. There is, therefore, little reason to suppose that radiotherapy, judged to be "adequate", prolongs life in Hodgkin's disease. For other types of reticulosis and for reticulosarcoma similar figures are not available, but there is no reason to suppose that they would show any striking difference.

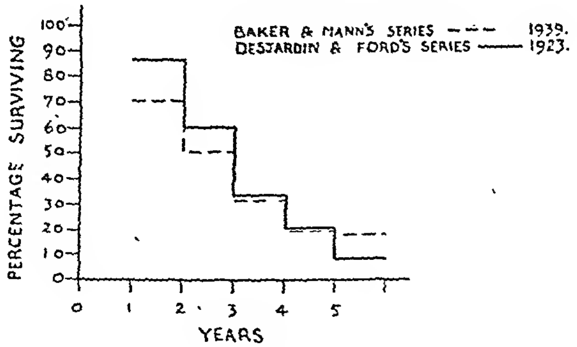


FIG. 1.—Percentage of patients with Hodgkin's disease surviving at the end of yearly periods.

No one would deny that radiotherapy is often followed by improvement in all these disorders, but this is transitory. Enlarged nodes disappear, fever vanishes, pruritus is controlled, and the patient's general health, for a time, shows great benefit.

From the point of view of treatment it is convenient to divide reticulosis and reticulosarcoma into two broad groups, depending on whether the disease is localized to one or two contiguous groups of lymph nodes, or is virtually systematized throughout the lympho-reticular tissue. Into the first category fall Hodgkin's disease, lympho-reticular, and many of the less common reticuloses and reticulosarcomata; into the second, lymphatic leukæmia, lymphoid follicular reticulosis, and lymphoblastic unhappy patients but they make it a little more tolerable. The benefits of radiotherapy are undoubtedly great, but I believe that this powerful weapon is sometimes used uncritically. When I see a patient in the terminal cachexia of Hodgkin's disease the thought often passes through my mind "how much of this is due to the disease process and how much to prolonged and intensive irradiation?"

REFERENCES

Baker, C., and Mann, W. N. (1939) *Guy's Hosp. Reps.*, 89, 83.
Desjardin, A. U., and Ford, F. A. (1923) *J. Amer. med. Assoc.*, 81, 925.

Professor M. J. Stewart: As to the effects of irradiation I had a case of Hodgkin's disease of the Pel-Ebstein type under observation some twenty years ago. The patient had himself kept a record for nearly two years of his night and morning temperature. Following the diagnosis of the disease after biopsy, he was sent to the Radium Institute in London for radiotherapy. This had very satisfactory results, practically all the superficial glands disappearing and the general state being much improved. Later, anæmia developed and there were signs of mediastinal involvement. The point of particular interest in the case was that in spite of the well-marked effect of the radiotherapy on the lymphadenopathy, the Pel-Ebstein phenomena continued, though in an altered form. There was some lowering of the temperature generally, but the bursts of "pyrexia", lasting four or five days, consisted of great *downward* fluctuations, the peaks rarely rising more than a degree or a degree and a half above normal.

Dr. E. Lipman Cohen: It has been reported that thorium X varnish has been useful in the symptomatic treatment of mycosis fungoides, it may also be of use in the relief of pruritus in Hodgkin's disease.

Professor D. W. Smithers: As the question of the treatment of mycosis fungoides by nitrogen mustard, methyl-bis (beta-chloroethyl) amine hydrochloride, has been raised, it is of interest to note that one such patient has been treated in this way at the Royal Cancer Hospital without any demonstrable effect.

Though X-ray therapy in the lymphadenopathies is only palliative, in some instances, at any rate, it is a very efficient means of palliation, and there can be little doubt that it does in some cases prolong life. One has only to see a case of giant follicular lymphadenopathy (lymphoid follicular reticulosis) with a large pleural effusion, and in a very poor state of general health, returned to normal life for a period sometimes of many years, as has already been pointed out, for this to strike one very forcibly.

The function of radiotherapy would seem to be that of relieving symptoms and returning the patient to a reasonable state of health for a while, and so giving opportunity for other methods of treatment to be used in the hope that some curative agent may be found.

Nothing has yet been said at this meeting about the use of radioactive isotopes. Perhaps there may be some future in the combination of chemotherapy on the lines now being investigated in combination with radioactive isotopes.

Surgeons still seem to have a not unnatural reluctance to remove regional lymph nodes in a generalized condition. The percentage of cases which have lymph node enlargement confined to one region, and which are amenable to surgery when first seen, is not large. I believe that a few cases have been treated with hyperpyrexia in this country, but so far I have heard of no favourable reports on this treatment.

secutive days. It appears to have a selective action on hæmopoietic tissue affecting, like X-irradiation, the lymphocytes first and most profoundly and the erythropoietic cells least. There is usually nausea and vomiting about four hours after the injection and anorexia for the four days on which the drug is administered. The leucocyte and platelet counts fall, reaching a minimum about fifteen days after the first dose, subsequent rise is rapid and usually complete by the twenty-fifth day; a small decrease in the erythrocyte count and the hæmoglobin level is also seen. One of my patients developed a scattered vesicular eruption fifteen days after the injection which lasted a week; a dermatologist regarded this as a sensitization effect. Other toxic effects are rare and there seem to have been no fatalities attributable to the drug.

Reports are guarded but the results in Hodgkin's disease appear better than in the other conditions in this group, and there are cases recorded which had become radioresistant but in which nitrogen mustard has induced temporary remission; it is, however, not curative. Even more impressive results have been obtained in mycosis fungoides.

My own experience of this compound is limited to its use in six recent cases: in these the immediate effects have been reduction in size of nodes, relief of severe abdominal pain in one, disappearance of fever in one. Its value remains to be assessed, but there are innumerable related compounds, one of which may prove to have a more selective action. If the effects of nitrogen mustard prove comparable to those of radiotherapy it will offer great advantages in the brief duration of treatment, the ease of administration, and the manner in which all diseased tissue is accessible to its action.

Another recently introduced chemotherapeutic agent is urethane. Of the diseases under discussion chronic lymphatic leukæmia is the only one in which it has a significant effect, and here the results are inconstant. A fall in the lymphocyte count and an improvement in the patient's general condition are often obtained but, although the enlarged lymph nodes decrease in size, they do not disappear. It can at best be regarded as an ineffectual form of symptomatic treatment.

I have discussed the main methods which are used in attempts to destroy the new formations which mark these diseases. The second aim of treatment is to maintain the patient's general health and control symptoms. It has been said that the patient is usually much benefited in the second respect when the first has been attained. But there comes a time in every case when the cachectic stage of the disorder begins: in those patients who have been irradiated palpable lymphadenopathy may no longer exist, there is progressive loss of weight, anæmia, weakness, fever, and particularly in Hodgkin's disease, obstinate pruritus. Radiotherapy is no longer effective and the resources of the physician are greatly taxed to make the patient's life tolerable.

Blood transfusion may control the anæmia in the more indolent cases, and may allow the patient to leave his bed. There are occasional instances where the salient symptom is hæmolytic anæmia or thrombocytopenic purpura secondary to the splenomegaly; in some of these splenectomy is justifiable as it may give the patient another year or more of fair health.

Pruritus is a particularly difficult problem. It often disappears when the local lesions have been adequately irradiated but in the later stages this form of treatment is no longer possible. Local applications are seldom effective. In some cases benadryl by mouth has given relief.

There is unfortunately no difficulty in showing that in these diseases the methods of treatment available to us are only symptomatic; they do not prolong life for these unhappy patients but they make it a little more tolerable. The benefits of radiotherapy are undoubtedly great, but I believe that this powerful weapon is sometimes used uncritically. When I see a patient in the terminal cachexia of Hodgkin's disease the thought often passes through my mind "how much of this is due to the disease process and how much to prolonged and intensive irradiation?"

REFERENCES

BAKER, C., and MANN, W. N. (1939) *Guy's Hosp. Reps.*, 89, 83.
DESJARDIN, A. U., and FORD, F. A. (1923) *J. Amer. med. Assoc.*, 81, 925.

Professor M. J. Stewart: As to the effects of irradiation I had a case of Hodgkin's disease of the Pel-Ebstein type under observation some twenty years ago. The patient had himself kept a record for nearly two years of his night and morning temperature. Following the diagnosis of the disease after biopsy, he was sent to the Radium Institute in London for radiotherapy. This had very satisfactory results, practically all the superficial glands disappearing and the general state being much improved. Later, anæmia developed and there were signs of mediastinal involvement. The point of particular interest in the case was that in spite of the well-marked effect of the radiotherapy on the lymphadenopathy, the Pel-Ebstein phenomena continued, though in an altered form. There was some lowering of the temperature generally, but the bursts of "pyrexia", lasting four or five days, consisted of great *downward* fluctuations, the peaks rarely rising more than a degree or a degree and a half above normal.

Dr. E. Lipman Cohen: It has been reported that thorium X varnish has been useful in the symptomatic treatment of mycosis fungoides, it may also be of use in the relief of pruritus in Hodgkin's disease.

Professor D. W. Smithers: As the question of the treatment of mycosis fungoides by nitrogen mustard, methyl-bis (beta-chloroethyl) amine hydrochloride, has been raised, it is of interest to note that one such patient has been treated in this way at the Royal Cancer Hospital without any demonstrable effect.

Though X-ray therapy in the lymphadenopathies is only palliative, in some instances, at any rate, it is a very efficient means of palliation, and there can be little doubt that it does in some cases prolong life. One has only to see a case of giant follicular lymphadenopathy (lymphoid follicular reticulosis) with a large pleural effusion, and in a very poor state of general health, returned to normal life for a period sometimes of many years, as has already been pointed out, for this to strike one very forcibly.

The function of radiotherapy would seem to be that of relieving symptoms and returning the patient to a reasonable state of health for a while, and so giving opportunity for other methods of treatment to be used in the hope that some curative agent may be found.

Nothing has yet been said at this meeting about the use of radioactive isotopes. Perhaps there may be some future in the combination of chemotherapy on the lines now being investigated in combination with radioactive isotopes.

Surgeons still seem to have a not unnatural reluctance to remove regional lymph nodes in a generalized condition. The percentage of cases which have lymph node enlargement confined to one region, and which are amenable to surgery when first seen, is not large. I believe that a few cases have been treated with hyperpyrexia in this country, but so far I have heard of no favourable reports on this treatment.

Dr. J. D. N. Nabarro: With regard to the use of the nitrogen mustards I have had the opportunity over the last ten months, under the direction of Professor H. P. Himsworth at University College Hospital, of using the "bis" salt in a number of cases. Six of these were previously untreated cases of Hodgkin's disease, the diagnosis being confirmed in each one by biopsy. In two there was no response to a single course of injections, in one the response was very slight, one is too recent to report and the other two showed satisfactory remissions. The first of these was a young woman with cervical and mediastinal glands, whose symptoms were abolished and general condition improved over a period of nine months, although the glands showed little change. She then had a relapse clinically and this was treated by deep X-ray therapy because the initial course of injections had been attended by such severe nausea and vomiting. The second satisfactory case was of particular interest, the patient was a middle-aged man with enlarged cervical glands and a very large liver and spleen. He ran a fever up to 102° F. and had a hæmoglobin level of 58%. After a course of injections his fever subsided by crisis and his hæmoglobin rose in three months to 100%. He had a febrile relapse two months later and his hæmoglobin fell to 57%, after another course it rose in two months to 90%. Unfortunately, he developed a bronchopneumonia shortly after from which he died. In this case, one not very suitable for X-ray therapy, nitrogen mustard produced two good remissions and enabled the patient to live an active life for some months.

There is no doubt that some cases of Hodgkin's disease show a definite response to this drug, but we have as yet no criteria on which we can foretell the result of treatment.

Section of Epidemiology and State Medicine

President—H. J. Parish, M.D., F.R.C.P.E., D.P.H.

[*February* 28, 1947]

DISCUSSION ON THE PRESENT STATUS OF INFECTIOUS DISEASE CONTROL IN CONTINENTAL EUROPE

Dr. Ian Taylor: The district for which I was responsible in Germany covered a distance of 50 or 60 miles north and south of the City of Hanover. Infectious disease control was only one of the many and varied duties which had to be carried out. It is convenient to discuss the subject under five headings:

(1) Environmental factors.
(2) Ascertainment of cases.
(3) Isolation and treatment.
(4) Action taken on notification.
(5) Specific prophylaxis.

(1) Environmental Factors: The city of Hanover had a pre-war population of about half a million. 60% of the dwellings in the city were either heavily damaged or totally destroyed, and most of the rest of the town had suffered some damage. The centre was just a heap of rubble, with only the main military routes cleared. Another sizeable town in the area, Hamelin, suffered about 12% of total damage. By comparison there was very little damage in the smaller towns and rural areas, except to bridges and main roads.

The total population of the area, about a million, and already considerably in excess of what it had been before the war, steadily increased after the war with the influx of refugees from other parts of Germany and New Poland, with the result that the average living space had shrunk when I left to 6·2 sq. metres (only about 70 sq. ft.) for living, eating and sleeping. I believe that the figure is now even smaller; and have recently heard that in spite of the fact that the city had been declared a black spot which could not receive refugees, they have now decided that it must receive a further increase of 10% in its population. The floating population of refugees, and to some extent residents, were frequently accommodated in huge concrete air-raid bunkers, some of which were below ground level, and which often held 3,000 or more persons. These places were quickly singled out as potential health hazards, and attempts made to prevent overcrowding and provide ventilation and health services.

There can be no doubt that a high proportion of the Germans are very hungry, and undernourishment is a factor that has to be considered by health workers in the British Zone.

In the city there were 600 breaks in the main sewers apart from minor damage to drains. In rainy weather they overflowed and the basements in certain areas became flooded.

Dr. J. D. N. Nabarro: With regard to the use of the nitrogen mustards I have had the opportunity over the last ten months, under the direction of Professor H. P. Himsworth at University College Hospital, of using the "bis" salt in a number of cases. Six of these were previously untreated cases of Hodgkin's disease, the diagnosis being confirmed in each one by biopsy. In two there was no response to a single course of injections, in one the response was very slight, one is too recent to report and the other two showed satisfactory remissions. The first of these was a young woman with cervical and mediastinal glands, whose symptoms were abolished and general condition improved over a period of nine months, although the glands showed little change. She then had a relapse clinically and this was treated by deep X-ray therapy because the initial course of injections had been attended by such severe nausea and vomiting. The second satisfactory case was of particular interest, the patient was a middle-aged man with enlarged cervical glands and a very large liver and spleen. He ran a fever up to 102° F. and had a hæmoglobin level of 58%. After a course of injections his fever subsided by crisis and his hæmoglobin rose in three months to 100%. He had a febrile relapse two months later and his hæmoglobin fell to 57%, after another course it rose in two months to 90%. Unfortunately, he developed a bronchopneumonia shortly after from which he died. In this case, one not very suitable for X-ray therapy, nitrogen mustard produced two good remissions and enabled the patient to live an active life for some months.

There is no doubt that some cases of Hodgkin's disease show a definite response to this drug, but we have as yet no criteria on which we can foretell the result of treatment.

provision for diphtheria in the shape of a special hutted hospital of 100 beds outside the town, and these beds are fully used. Even so, I gathered that they regard it as quite normal for a considerable proportion of diphtheria cases to be nursed at home.

The treatment of cases in hospital suffered considerably from the shortage of drugs and dressings. Treatment of diphtheria and antitoxin dosage differed little from that in this country.

Sulphonamides of all sorts were extremely short after the capitulation, owing to the fact that industrial production was curtailed. We issued sulphonamide on the strict understanding that the drug would be used for the treatment of venereal disease only. It was naturally difficult for the Germans to understand why sulphonamide could not be issued also for the saving of life in other diseases, and this situation resulted in a number of heartbreaking interviews in the office. But it was a matter of high policy, and had to be accepted.

Penicillin was not available for Germans, although in the spring of 1946 a quantity was released, again on the understanding that it was for the treatment of sulphonamide-resistant gonorrhœa.

(4) Action taken on Notification: The organization required for investigation of the source of infection in local outbreaks was sadly defective. This was due, in part, to the fact that there were no persons on the staff of the public health departments of the exact status and training of our sanitary inspectors. Most of the sanitary inspection as such was left to the various branches of the police. It is true that each Kreis had one or two men on the staff who were known as "disinfectors" but their duties, as far as I could discover, were limited to what the name implies. The detailed enquiry into the circumstances of infection fell to a great extent upon the M.O.H. in person. Many of them were strangely apathetic in the matter, even when cases of typhus arose, and in the early days it was only because we were continually on their tail that they were stimulated to the necessary action in disinfestation of contacts. It became necessary at a later stage to require the M.O.H. to give us within twenty-four hours a full report on each case of typhus, giving particulars of the presumed source of infection, and the action taken with contacts, and we were thus able to check the fact that action had been taken. In view of the extreme importance of immediate and thorough dusting of typhus contacts, we issued a quantity of D.D.T. fairly early on to each Kreis, and the Kreis disinfector was given instruction in its use.

In addition to the M.O.H. there were, in certain widely separated places, so-called "Hygienic Institutes", which were bacteriological laboratories doing a certain amount of public health work. They were supposed to have a function in the investigation of epidemic diseases, but the areas they covered were far too large for any real activity except in the immediate locality. This remoteness from practical reality was shown up very clearly when I heard that the professor in charge of the laboratory in Hanover, whose area of influence included that part of the country in which Belsen is situated, was able to persuade the authorities that he had no knowledge of what was going on there.

Almost the first serious trouble to occur after arrival was a considerable outbreak of poliomyelitis in a town of 10,000 inhabitants. I think that the unusual course that was taken in putting the town into complete quarantine did help to limit the infection to that town.

(5) Specific Prophylaxis: *Diphtheria.*—Immunization against diphtheria was not compulsory under the Nazis, although there was power to make it so locally as deemed necessary, and only certain districts had done so.

The figures for the British Zone for September 1946 show that diphtheria morbidity was 45·4 per 10,000 per week, which is between three and four times the pre-war September figure which averaged 13·6 from 1928 to 1938. In my own area during the period July to December 1945 the average was 27·35 per 10,000.

In reconciling the level of diphtheria with the supposedly high degree of inoculation it is worth while taking note of certain facts. In 1945 when I called for a report on diphtheria immunization in the area it emerged that the last general inoculation had taken place in 1943 (two years previously) when 37,000 school children and 35,000 children under 6 had been inoculated. Of this total of 72,000 children, only 58,000 received the second injection. The following year they switched over to combined diphtheria and scarlet fever immunization, and only 628 children were inoculated—this in a community that had more than 5,000 births each year. These figures are an interesting commentary on totalitarian methods in practice. It seems to be the old story of relying more on periodic mass attack on the population than on arrangements for systematic treatment of the individual child, with the usual resulting

The water in the city came from four waterworks. Two of these drew their water from the River Leine, and the water from these was chlorinated normally. Two others took water from wells in a peat bog about 25 km. north of the town and the Germans were very proud of the purity of this supply. In view of the impossibility of guaranteeing freedom from pollution in the damaged distribution system we had to insist on chlorination. They were very reluctant to institute it, and took it almost as a personal insult to their intelligence. However in February 1946, when the worst floods in living memory occurred, and the River Leine, with a normal width of 30 ft. in the centre of the town, became a raging torrent a quarter of a mile wide, submerging parts of the town, severing communications, isolating some of the hospitals, and incidentally submerging two of the waterworks, it was a great comfort to know that whatever was happening in the pipes and drains below ground, no water was being delivered from the two waterworks that were still functioning without being superchlorinated.

Soap was extremely scarce and poor in quality. No coal was available for producing hot water in the home. These two factors, coupled with the existing overcrowding, were probably responsible for the high incidence of scabies, although the degree of infestation with pediculosis was less than one would have expected.

The background of undernourishment and overcrowding presented a very black picture when one considered the risk of spread of typhus, a disease that was constantly being introduced by refugees coming from the East.

The process of denazification of the medical services, although necessary, undoubtedly lowered the general level of public health work and the standard of skill in the specialties in the large hospitals. There was a surfeit of doctors of mediocre attainments, but first-class specialists were hard to find.

(2) ASCERTAINMENT OF CASES: At the time of the fall of Germany there was no organized system of collection of infectious diseases intelligence relating to the German population. The reason for this lack was the complete disorganization of civilian telegraphs, telephones and road and rail transport.

We put into operation at once a scheme whereby the Burgomaster or Landrat in each county district had to supply to the local Military Government administrative officer each week a statement of the number of cases and deaths from infectious diseases in the area in the previous week. These were sent up by Military Government courier to our office, where they were consolidated and sent on to higher levels, with copies to the heads of the medical services of the local British troops. For a long time these were the only returns for infectious diseases available, and formed the basis of the consolidated returns circulated centrally by UNRRA and the Ministry of Health.

Attempts were, however, made to put the responsibility for collecting information on to the German machine as soon as possible. But even when I left Germany in April 1946 I was still able to get a weekly consolidated statement forty-eight hours before my opposite number in the German administration, as he was still being hampered by inadequate civilian communications.

The return included the usual notifiable diseases. Additions to the list that were made by us at various times were venereal diseases (by sexes), influenza, pneumonia, and scabies.

Orders were given that cases of typhus, smallpox, plague, cholera, and relapsing fever, besides being included in the weekly list, were to be the subject of an immediate telegraphic report. Typhus was the only one of these diseases which occurred, and the system worked quite well, although at the beginning there was some confusion over the German word "typhus" and more than once I made a fifty-mile car journey to investigate a case of typhus which on enquiry turned out to be typhoid. By a later order, louse-borne typhus, when referred to, was always followed by the German term "fleckfieber" and this innovation worked remarkably well in preventing confusion.

(3) ISOLATION AND TREATMENT: In the Hanover district it was customary for cases of infectious diseases to be received into special infectious blocks in the municipal general hospitals. The standard of isolation accommodation varied in different districts, but normally was of the standard provided in England at the end of the last century. An exception to this was the infectious section of the City hospital at Hanover, which was more pretentious, and included a modern block of single-bedded cubicles. This had been a very good block until it was practically put out of action by Allied air raids.

An interesting sidelight on the present incidence of diphtheria is that whereas in Hanover the city municipal hospital has 400 infectious diseases beds, they have had to make emergency

Dr. H. Stanley Banks: *Experiences in South Italy, Jugoslavia and the U.S. Zone of Germany.*—In spite of my having spent twenty-one months in Continental Europe, I fear that any information I can give on infectious disease control will be incomplete and only approximately correct. This is the result of the incredible state of disorganization of the countries concerned, of their paucity of trained staffs, of the absence of wartime and post-war records, and of the extreme difficulties of communication and transport.

SOUTH ITALY: *Typhus fever* was effectively snuffed out by the use of D.D.T. in the Naples outbreak of January 1944; *typhoid fever* was relatively abundant in the civil population and very rare among the well-inoculated troops; *bacillary dysentery* was abundant in both and controlled. in the Army, only partially by hygienic measures and largely by early treatment with sulphonamide drugs; *smallpox* flared up in several villages and small towns—these were quarantined and put out of bounds to troops for several months; *malaria* was controlled by the new method of adult mosquito control (as distinct from larval control) by D.D.T. spraying of certain buildings where mosquitoes are found. On these subjects much has already been written. A few moments might, however, be devoted to *diphtheria* in the forces in Italy. The amount of mild and moderate tonsillar diphtheria, cutaneous diphtheria and diphtheritic neuritis following missed cases encountered in the forces, was, I think, somewhat of a surprise to the Army Medical Authorities. At the Army Physicians' Conference in Rome in January 1945 many of the medical specialists exhibited some confusion and uncertainty as to the pathogenesis and treatment of diphtheria. Even the use of antitoxin was not always thoroughly understood. Several of the American physicians, in particular, admitted that, prior to this, they had never seen a case of the disease. It was evident that medical inexperience of diphtheria was a far from negligible factor in the problem.

The prevalence of diphtheria in the field raised the question of prophylaxis by mass Schick testing and immunization of the whole of the British forces in the area. This was rejected, however, as a practical impossibility. The question has been discussed by Brigadier J. S. K. Boyd (1946) and the conclusion reached that Schick testing and immunization should be done at the recruiting stage, and not in the field. I understand, however, that the relatively small New Zealand and Canadian forces did manage to achieve active immunization in the field. We must here pay tribute to the prescience of G. Ramon (1945). He secured, largely by personal influence, the active immunization of the French Army against diphtheria as early as 1936. This measure paid handsome dividends when hundreds of thousands of French prisoners of war were subjected to severe diphtheria infection in prisoner of war camps in Germany and experienced a very small morbidity as compared with that of Belgian prisoners of war in the same camps. The failure to immunize the British Army against diphtheria at the recruiting stage before or during the war appears to have been a major omission in an otherwise remarkably well-planned Army programme of prophylaxis against disease.

JUGOSLAVIA.—Let me sketch in outline the background of the picture. It is a country grossly despoiled of its medical and hospital equipment; so short of doctors and nurses that in places there was only one doctor to about 30,000 of population; the medical administration is poor, sketchy and completely subservient to political ideas and political bosses; and yet we have here a virile peasantry and people accustomed to hard conditions and often bearing extreme privations without complaint. Wherever I went, I visited the hospitals. They were overcrowded and lacking in food, clothing and equipment to a degree difficult even to imagine. In the Civil Hospital, Split, an adapted building, there were, in February 1945, literally 400 cases in 250 beds. In the State General Hospital, Belgrade, in April 1945, there were literally 850 patients in 500 beds. That means that in each ward of 12 to 16 beds there were two or three beds each with two occupants. Every child's bed, of course, contained two children, "tops and tails"; a number of women's beds were similarly "doubled"; but it was an incredible sight to see two sick men side by side in a narrow hospital bed, spending their days and nights balanced precariously just inside the rails. In most hospitals there were very few blankets or sheets, just coats or scrap-up bed clothing brought in by the patients themselves; no X-ray films, no rubber gloves, little or no anæsthetics, few needles, syringes, instruments, drugs or even sutures.

Smallpox.—The control of smallpox in Jugoslavia is very efficient owing to universal vaccination at the age of 3 months or thereabouts and universal re-vaccination at 6 years and again on entering the Services. The disease has been completely absent from the country since 1930. The vaccination scheme has perforce been suspended since 1941. The vaccinations in the rural areas are carried out by village hygiene teams of lay workers who undergo a few weeks' whole-time training in this and other practical hygiene measures at the District Hygiene Institutes. In May 1945 two cases of smallpox were reported but the diagnosis was

difficulty in assessing the mass immunity of the population at any given time. It is noteworthy also that the prophylactic in use in that district was a combination in one injection of alum precipitated diphtheria toxoid with alum precipitated scarlet fever toxoid.

On the other hand, the fact that diphtheria immunization may be taking effect in Germany is suggested by a considerable rise in the average age of attack, a phenomenon which we have come to associate, rightly or wrongly, with the development of some degree of mass immunity in the child population. It may well be that the present high level of diphtheria in Germany is due to a mixture of patchy immunization technique and enhanced virulence and infectivity of the organism.

Typhus.—A number of vaccines were in use in the early period. I believe that Weigl's vaccine was being made in Hamburg, but saw nothing of its use. The commonest vaccine was a mouse-lung vaccine. The main threat of typhus after the initial clear-up was the stream of refugees coming from the New Poland. All who came through the transit camps had been properly dusted with D.D.T. both there and on the journey. Such cases as occurred were almost without exception infected outside the British Zone, and the threat was therefore greatest to public health officials and hospital staff who might become directly involved in handling these imported cases. It was therefore decided to immunize this special group of health workers. This decision coincided with reports of the infection of certain hospital workers who had been vaccinated, and in subsequent vaccination only egg-yolk vaccine was used.

Smallpox.—Smallpox vaccination is on a firmer footing than diphtheria immunization. It is compulsory for all in infancy. The only exception is when the health of the child would be prejudiced by vaccination, and vaccination is not excused in these cases, but merely postponed. Conscientious objection is not allowed. Re-vaccination of older children between the ages of 10 and 12 years is also compulsory. I cannot help feeling that although there is not much to admire in present-day Germany, we can envy the vaccinal state of their population.

Intestinal diseases.—During my stay in Hanover enteric fever was occurring at the rate of about 20 cases per million per week. The great majority of the infections were typhoid fever, with a sprinkling of paratyphoid A. These cases arose sporadically. Other districts in the Zone were experiencing a considerably higher incidence, and in certain places localized outbreaks of considerable proportions were reported, which raised the suspicion of infection of rural water supplies.

Dysentery figures were much lower than those of typhoid, which was surprising in view of the overcrowding and shortage of soap and hot water. At no time did we have the difficulties with dysentery that were described by the public health officers from Berlin at a previous meeting (*Proc. R. Soc. Med.*, **40**, 89).

In view of the high general incidence of typhoid and the unsatisfactory sanitary background, a general inoculation of the population with TAB was ordered and was in progress when I came home. From this distance I suppose that it is possible to question its wisdom. When in the midst of the problem, however, with high enteric incidence, grossly defective public and domestic hygiene, with little prospect of immediate improvement in environmental conditions, the case seemed very strong. As might be expected, reports from some districts that incidence has been reduced have been accompanied by statements that certain individuals incubating the disease had been killed by inoculations.

It may be said that infectious disease control in the circumstances described will remain a nightmare for health workers in the Zone for a long time to come.

Wholesale chlorination of main water in the larger centres and the use of D.D.T. to control imported typhus have probably played a very great part in success so far achieved.

Immunization against various diseases may also have played some part.

Good fortune has also played a not inconsiderable part, and a widespread outbreak of respiratory disease in the malnourished, overcrowded population, with such poor hospital facilities, so inadequately supplied with medicaments, would tax resources to the utmost.

The problem of tuberculosis, which is now coming to the stage when it can be treated as a priority, will undoubtedly present enormous difficulties.

In conclusion I feel that I cannot do better than quote the words of Geddes Smith in his admirable and fascinating book, "Plague on Us", published in America in 1940:

> "The lords of Europe are fighting again. Masses of men are bombed out of their homes and cities, hounded into exile, driven hither and thither, in a greater dislocation of ordered living than any rational man would have thought possible. Such a world is in peril of pestilence. It is early to boast."

Dr. H. Stanley Banks: *Experiences in South Italy, Jugoslavia and the U.S. Zone of Germany.*—In spite of my having spent twenty-one months in Continental Europe, I fear that any information I can give on infectious disease control will be incomplete and only approximately correct. This is the result of the incredible state of disorganization of the countries concerned, of their paucity of trained staffs, of the absence of wartime and post-war records, and of the extreme difficulties of communication and transport.

SOUTH ITALY: *Typhus fever* was effectively snuffed out by the use of D.D.T. in the Naples outbreak of January 1944; *typhoid fever* was relatively abundant in the civil population and very rare among the well-inoculated troops; *bacillary dysentery* was abundant in both and controlled, in the Army, only partially by hygienic measures and largely by early treatment with sulphonamide drugs; *smallpox* flared up in several villages and small towns—these were quarantined and put out of bounds to troops for several months; *malaria* was controlled by the new method of adult mosquito control (as distinct from larval control) by D.D.T. spraying of certain buildings where mosquitoes are found. On these subjects much has already been written. A few moments might, however, be devoted to *diphtheria* in the forces in Italy. The amount of mild and moderate tonsillar diphtheria, cutaneous diphtheria and diphtheritic neuritis following missed cases encountered in the forces, was, I think, somewhat of a surprise to the Army Medical Authorities. At the Army Physicians' Conference in Rome in January 1945 many of the medical specialists exhibited some confusion and uncertainty as to the pathogenesis and treatment of diphtheria. Even the use of antitoxin was not always thoroughly understood. Several of the American physicians, in particular, admitted that, prior to this, they had never seen a case of the disease. It was evident that medical inexperience of diphtheria was a far from negligible factor in the problem.

The prevalence of diphtheria in the field raised the question of prophylaxis by mass Schick testing and immunization of the whole of the British forces in the area. This was rejected, however, as a practical impossibility. The question has been discussed by Brigadier J. S. K. Boyd (1946) and the conclusion reached that Schick testing and immunization should be done at the recruiting stage, and not in the field. I understand, however, that the relatively small New Zealand and Canadian forces did manage to achieve active immunization in the field. We must here pay tribute to the prescience of G. Ramon (1945). He secured, largely by personal influence, the active immunization of the French Army against diphtheria as early as 1936. This measure paid handsome dividends when hundreds of thousands of French prisoners of war were subjected to severe diphtheria infection in prisoner of war camps in Germany and experienced a very small morbidity as compared with that of Belgian prisoners of war in the same camps. The failure to immunize the British Army against diphtheria at the recruiting stage before or during the war appears to have been a major omission in an otherwise remarkably well-planned Army programme of prophylaxis against disease.

JUGOSLAVIA.—Let me sketch in outline the background of the picture. It is a country grossly despoiled of its medical and hospital equipment; so short of doctors and nurses that in places there was only one doctor to about 30,000 of population; the medical administration is poor, sketchy and completely subservient to political ideas and political bosses; and yet we have here a virile peasantry and people accustomed to hard conditions and often bearing extreme privations without complaint. Wherever I went, I visited the hospitals. They were overcrowded and lacking in food, clothing and equipment to a degree difficult even to imagine. In the Civil Hospital, Split, an adapted building, there were, in February 1945, literally 400 cases in 250 beds. In the State General Hospital, Belgrade, in April 1945, there were literally 850 patients in 500 beds. That means that in each ward of 12 to 16 beds there were two or three beds each with two occupants. Every child's bed, of course, contained two children, "tops and tails"; a number of women's beds were similarly "doubled"; but it was an incredible sight to see two sick men side by side in a narrow hospital bed, spending their days and nights balanced precariously just inside the rails. In most hospitals there were very few blankets or sheets, just coats or scrap-up bed clothing brought in by the patients themselves; no X-ray films, no rubber gloves, little or no anæsthetics, few needles, syringes, instruments, drugs or even sutures.

Smallpox.—The control of smallpox in Jugoslavia is very efficient owing to universal vaccination at the age of 3 months or thereabouts and universal re-vaccination at 6 years and again on entering the Services. The disease has been completely absent from the country since 1930. The vaccination scheme has perforce been suspended since 1941. The vaccinations in the rural areas are carried out by village hygiene teams of lay workers who undergo a few weeks' whole-time training in this and other practical hygiene measures at the District Hygiene Institutes. In May 1945 two cases of smallpox were reported but the diagnosis was

difficulty in assessing the mass immunity of the population at any given time. It is noteworthy also that the prophylactic in use in that district was a combination in one injection of alum precipitated diphtheria toxoid with alum precipitated scarlet fever toxoid.

On the other hand, the fact that diphtheria immunization may be taking effect in Germany is suggested by a considerable rise in the average age of attack, a phenomenon which we have come to associate, rightly or wrongly, with the development of some degree of mass immunity in the child population. It may well be that the present high level of diphtheria in Germany is due to a mixture of patchy immunization technique and enhanced virulence and infectivity of the organism.

Typhus.—A number of vaccines were in use in the early period. I believe that Weigl's vaccine was being made in Hamburg, but saw nothing of its use. The commonest vaccine was a mouse-lung vaccine. The main threat of typhus after the initial clear-up was the stream of refugees coming from the New Poland. All who came through the transit camps had been properly dusted with D.D.T. both there and on the journey. Such cases as occurred were almost without exception infected outside the British Zone, and the threat was therefore greatest to public health officials and hospital staff who might become directly involved in handling these imported cases. It was therefore decided to immunize this special group of health workers. This decision coincided with reports of the infection of certain hospital workers who had been vaccinated, and in subsequent vaccination only egg-yolk vaccine was used.

Smallpox.—Smallpox vaccination is on a firmer footing than diphtheria immunization. It is compulsory for all in infancy. The only exception is when the health of the child would be prejudiced by vaccination, and vaccination is not excused in these cases, but merely postponed. Conscientious objection is not allowed. Re-vaccination of older children between the ages of 10 and 12 years is also compulsory. I cannot help feeling that although there is not much to admire in present-day Germany, we can envy the vaccinal state of their population.

Intestinal diseases.—During my stay in Hanover enteric fever was occurring at the rate of about 20 cases per million per week. The great majority of the infections were typhoid fever, with a sprinkling of paratyphoid A. These cases arose sporadically. Other districts in the Zone were experiencing a considerably higher incidence, and in certain places localized outbreaks of considerable proportions were reported, which raised the suspicion of infection of rural water supplies.

Dysentery figures were much lower than those of typhoid, which was surprising in view of the overcrowding and shortage of soap and hot water. At no time did we have the difficulties with dysentery that were described by the public health officers from Berlin at a previous meeting (*Proc. R. Soc. Med.*, 40, 89).

In view of the high general incidence of typhoid and the unsatisfactory sanitary background, a general inoculation of the population with TAB was ordered and was in progress when I came home. From this distance I suppose that it is possible to question its wisdom. When in the midst of the problem, however, with high enteric incidence, grossly defective public and domestic hygiene, with little prospect of immediate improvement in environmental conditions, the case seemed very strong. As might be expected, reports from some districts that incidence has been reduced have been accompanied by statements that certain individuals incubating the disease had been killed by inoculations.

It may be said that infectious disease control in the circumstances described will remain a nightmare for health workers in the Zone for a long time to come.

Wholesale chlorination of main water in the larger centres and the use of D.D.T. to control imported typhus have probably played a very great part in success so far achieved.

Immunization against various diseases may also have played some part.

Good fortune has also played a not inconsiderable part, and a widespread outbreak of respiratory disease in the malnourished, overcrowded population, with such poor hospital facilities, so inadequately supplied with medicaments, would tax resources to the utmost.

The problem of tuberculosis, which is now coming to the stage when it can be treated as a priority, will undoubtedly present enormous difficulties.

In conclusion I feel that I cannot do better than quote the words of Geddes Smith in his admirable and fascinating book, "Plague on Us", published in America in 1940:

> "The lords of Europe are fighting again. Masses of men are bombed out of their homes and cities, hounded into exile, driven hither and thither, in a greater dislocation of ordered living than any rational man would have thought possible. Such a world is in peril of pestilence. It is early to boast."

Dr. H. Stanley Banks: *Experiences in South Italy, Jugoslavia and the U.S. Zone of Germany.*—In spite of my having spent twenty-one months in Continental Europe, I fear that any information I can give on infectious disease control will be incomplete and only approximately correct. This is the result of the incredible state of disorganization of the countries concerned, of their paucity of trained staffs, of the absence of wartime and post-war records, and of the extreme difficulties of communication and transport.

SOUTH ITALY: *Typhus fever* was effectively snuffed out by the use of D.D.T. in the Naples outbreak of January 1944 ; *typhoid fever* was relatively abundant in the civil population and very rare among the well-inoculated troops; *bacillary dysentery* was abundant in both and controlled, in the Army, only partially by hygienic measures and largely by early treatment with sulphonamide drugs; *smallpox* flared up in several villages and small towns—these were quarantined and put out of bounds to troops for several months; *malaria* was controlled by the new method of adult mosquito control (as distinct from larval control) by D.D.T. spraying of certain buildings where mosquitoes are found. On these subjects much has already been written. A few moments might, however, be devoted to *diphtheria* in the forces in Italy. The amount of mild and moderate tonsillar diphtheria, cutaneous diphtheria and diphtheritic neuritis following missed cases encountered in the forces, was, I think, somewhat of a surprise to the Army Medical Authorities. At the Army Physicians' Conference in Rome in January 1945 many of the medical specialists exhibited some confusion and uncertainty as to the pathogenesis and treatment of diphtheria. Even the use of antitoxin was not always thoroughly understood. Several of the American physicians, in particular, admitted that, prior to this, they had never seen a case of the disease. It was evident that medical inexperience of diphtheria was a far from negligible factor in the problem.

The prevalence of diphtheria in the field raised the question of prophylaxis by mass Schick testing and immunization of the whole of the British forces in the area. This was rejected, however, as a practical impossibility. The question has been discussed by Brigadier J. S. K. Boyd (1946) and the conclusion reached that Schick testing and immunization should be done at the recruiting stage, and not in the field. I understand, however, that the relatively small New Zealand and Canadian forces did manage to achieve active immunization in the field. We must here pay tribute to the prescience of G. Ramon (1945). He secured, largely by personal influence, the active immunization of the French Army against diphtheria as early as 1936. This measure paid handsome dividends when hundreds of thousands of French prisoners of war were subjected to severe diphtheria infection in prisoner of war camps in Germany and experienced a very small morbidity as compared with that of Belgian prisoners of war in the same camps. The failure to immunize the British Army against diphtheria at the recruiting stage before or during the war appears to have been a major omission in an otherwise remarkably well-planned Army programme of prophylaxis against disease.

JUGOSLAVIA.—Let me sketch in outline the background of the picture. It is a country grossly despoiled of its medical and hospital equipment; so short of doctors and nurses that in places there was only one doctor to about 30,000 of population; the medical administration is poor, sketchy and completely subservient to political ideas and political bosses; and yet we have here a virile peasantry and people accustomed to hard conditions and often bearing extreme privations without complaint. Wherever I went, I visited the hospitals. They were overcrowded and lacking in food, clothing and equipment to a degree difficult even to imagine. In the Civil Hospital, Split, an adapted building, there were, in February 1945, literally 400 cases in 250 beds. In the State General Hospital, Belgrade, in April 1945, there were literally 850 patients in 500 beds. That means that in each ward of 12 to 16 beds there were two or three beds each with two occupants. Every child's bed, of course, contained two children, "tops and tails"; a number of women's beds were similarly "doubled"; but it was an incredible sight to see two sick men side by side in a narrow hospital bed, spending their days and nights balanced precariously just inside the rails. In most hospitals there were very few blankets or sheets, just coats or scrap-up bed clothing brought in by the patients themselves; no X-ray films, no rubber gloves, little or no anæsthetics, few needles, syringes, instruments, drugs or even sutures.

Smallpox.—The control of smallpox in Jugoslavia is very efficient owing to universal vaccination at the age of 3 months or thereabouts and universal re-vaccination at 6 years and again on entering the Services. The disease has been completely absent from the country since 1930. The vaccination scheme has perforce been suspended since 1941. The vaccinations in the rural areas are carried out by village hygiene teams of lay workers who undergo a few weeks' whole-time training in this and other practical hygiene measures at the District Hygiene Institutes. In May 1945 two cases of smallpox were reported but the diagnosis was

not confirmed. Nevertheless, an attempt was made to get the machinery of vaccination going again. I had the task of organizing the import by air of half a million doses of vaccine from the Middle East. In spite of the clearest instructions, however, most of this material was wasted owing to inadequate storage in the hot weather. In Belgrade there was a 30% take, but in Macedonia, where storage conditions were very primitive, only a 1% take was obtained. I saw no case of smallpox in Jugoslavia. The immunity of the country from smallpox may be, I think, fairly attributed to the highly vaccinated and re-vaccinated state of the population. No accurate data exist as to the prevalence of post-vaccinal encephalitis.

Typhus fever.—All the indications pointed to typhus fever as the greatest epidemic danger to post-war Europe. This disease has been endemic in Jugoslavia, particularly in Bosnia, since the first World War. In 1942-43 there was a flare-up with some thousands of cases reported in the country. In the first few months of 1945, some 5,000 to 7,000 cases were reported per month, and even as late as June 1945 the figure for the month was 1,000 cases. In the twelve months from January 1945 to January 1946 no less than 40,000 cases were reported in Jugoslavia. The disease was, therefore, at this time just held in check and no more. Most of the cases during the war occurred in and around the area of operations of the Jugoslav Army. There is evidence that the disease was controlled to a considerable extent by the simple methods employed by the hygiene sections of the Jugoslav Army. These consisted chiefly in the regular use of the Serbian barrel steam disinfector for soldiers' clothing, a method introduced by Zinsser during the Serbian epidemic of 1915. Control became easier when D.D.T. was brought into the country by the U.S. Typhus Commission in February 1945. By January 1946, nearly ½ million pounds of D.D.T. powder had been delivered to Jugoslavia by the Typhus Commission and UNRRA. But the bulk of this was too late for the rush of refugees that passed through the country during the two or three months following the end of the war. Typhus control in Europe at this period was almost entirely due to the D.D.T. disinfestation stations which were set up by the Army at various points on the frontiers of Germany and Austria.

A noble attempt to mass-inoculate the whole population of Bosnia with anti-typhus vaccine was commenced in May 1945 by the Typhus Commission, and continued under the supervision of the medical staff of the Hygiene Institute of Sarajevo. The inoculations were done by no less than 170 teams of four or more lay workers who had each received some two weeks' training. The scheme was interrupted several times by lack of materials and also by poor staff work at the Ministry of Health in Belgrade. It is estimated, however, that some 800,000 of the two million inhabitants of Bosnia received one or more inoculations. These anti-typhus inoculations were believed to have three main effects: (1) reduction of the mortality of the disease (even in old people) to almost nil; (2) reduction of morbidity and therefore also of the number of infective persons; and (3) reduction of the number of infective lice. This experiment was never completed and did not succeed in its object of eradicating the endemic foci of typhus in Bosnia. Nevertheless, thanks to this and to the liberal use of D.D.T. for disinfestation during the winter succeeding the war, the danger of epidemic typhus spreading from Jugoslavia to the rest of Europe was completely overcome. In this achievement it is hardly to be doubted that D.D.T. deserves the major share of the credit.

Tuberculosis.—Throughout Europe the problem of tuberculosis is probably the greatest in the whole field of public health. The incidence and death-rates of tuberculosis in Jugoslavia are very comparable to those recently estimated for Poland by Marc Daniels (1946). In 1944, the deaths from all forms of tuberculosis in the town of Split were at the rate of 300 per 100,000 population, the same figure as that for Lodz in Poland. In the whole of Croatia, T.B. deaths were estimated in July 1945 at 400 per 100,000 population or about eight times the death-rate from tuberculosis in Britain. This represents more than a twofold increase over Jugoslavia's pre-war tuberculosis death-rate which was one of the highest in Europe. An attempt was made to obtain data from a mass radiography survey. After tremendous trouble by UNRRA officials a set of limited power was obtained from Italy and put in the charge of an excellent technician. The Jugoslav authorities, however, with typical Jugoslav recklessness, insisted on running the machine far in excess of its capacity, with the result that it was wrecked in a week. This is the reason for the complete absence of data from mass radiography in Jugoslavia.

Hardly any effective control of tuberculosis is being exercised in Jugoslavia. Clinic, hospital and sanatorium services are grossly inadequate. Poverty and underfeeding are general throughout the country as well as in the hospitals. Nothing less than a substantial rise in the standard of living of the whole population is likely to bring about an improvement.

Venereal diseases.—In Bosnia syphilis is said to be prevalent to the extent of 10% of the population. No exact estimate is, however, possible, owing to the absence of reliable sampling surveys. Dr. Grin of the Sarajevo Hygiene Institute believes that the disease is not only venereal, but frequently transmitted by the use of common food utensils among families and units containing members with acute nasopharyngeal and oral lesions. Knowing the habits of the peasantry, I think this may be quite a likely source of infection.

Intestinal diseases.—As in Italy, *bacillary dysentery* is endemic. In summer practically everyone in Jugoslavia has several attacks of it. Those of us who were able to obtain supplies of sulphaguanidine controlled our attacks by its regular use at the first onset of diarrhœa. The Jugoslavs, in 1945 at least, just suffered until they acquired enough natural immunity to tide them over until the next attack.

Typhoid fever is also very rife. Our six-monthly T.A.B. inoculation was, without doubt, the source of our personal immunity. The worst area is probably Macedonia, since there hygiene is the most primitive. Water supplies, usually springs and shallow wells, are in bad repair. The privy and open well often exist in the same yard. The sewage is often carried in the street gutters. Morbidity from intestinal diseases in Macedonia is estimated at 30% and mortality at 10%. No effective help could be given with this problem by the UNRRA sanitary engineering section, owing to lack of co-operation from the Ministry of Health. The latter's policy was entirely dominated by the political and military factors in the situation.

Malaria.—At a conference of malariologists in Belgrade in April 1946 it was estimated that there were 1,200,000 cases of malaria in the country per annum. In Macedonia over 30% of the population of one million suffer from malaria. Again, no effective help could be given with this problem because the authorities would neither allow proper surveys to be made nor allocate skilled staff to operate the plant which, in the beginning, was supplied. In Greece, UNRRA supplied aeroplanes for spraying marshy land with D.D.T. The Jugoslav authorities demanded aeroplanes also, but as there was every reason to think that the planes would have been used for military purposes, they were not supplied. And so, although UNRRA sent a strong sanitary engineering section into the country, and were prepared to supply large quantities of anti-malaria materials, it proved impossible to make any effective contribution to anti-malarial work, owing to the intransigent attitude of the Government.

Nursing.—Six highly skilled U.S. and British public health nurses laboured for over a year in the country trying to organize the training of nurses. Their labours were in vain. Finally, it was arranged to provide fellowships for training of 20 nurse-teachers in U.S.A. The 20 candidates were selected by the Government (with, of course, the usual political considerations in mind). Out of the 20, visas were allotted to 18 and the other two were refused. The Jugoslav authorities were so incensed at this refusal that they called off the whole scheme. Thus the nursing contribution of UNRRA to infectious disease control ended in failure.

UNRRA supplies.—In spite of such rebuffs, by September 1946 UNRRA, under the leadership of a Russian chief of mission, had imported into Jugoslavia no less than two million tons of supplies, including vast quantities of medical and hospital supplies. The whole of this was a free gift to the Jugoslav Government. Acknowledgment took the form of the usual elaborate feast to the UNRRA officials, but (to quote the official report) "the foreign policy of the Government forbade all public recognition of this unprecedented gift".

GERMANY: I can make only very brief reference to the U.S. Zone of Germany. Infectious disease, except tuberculosis, among the displaced persons is remarkably low, thanks to regular inoculations against diphtheria, smallpox, typhus and typhoid fevers, to regular D.D.T. dustings and to a reasonably good diet, which is supposed to include approximately 1,000 calories from fresh meat, milk, eggs, &c. On the other hand, large epidemics of *typhoid fever* occur among German civilians. In one district of Bavaria from September to November 1946, there were 2,500 cases of typhoid reported among German civilians, while there were only 8 cases among the thousands of displaced persons in the area—another tribute to the preventive effects of regular T.A.B. vaccine.

Tuberculosis is worst in the Jewish camps, although the incidence is now much less than it was at the close of the war. Mass radiography in the Jewish camps shows a rate of about 2% active tuberculosis based on examination of 35 mm. film only. This figure would probably be considerably reduced after hospital observation of doubtful cases. Tuberculosis hospital and sanatorium provision is of course inadequate, but probably less so for both D.P.s and civilians in Germany than in many other countries in Europe.

REFERENCES

BOYD, J. S. K. (1946) *Lancet* (ii), 195.
DANIELS, M. (1946) *Lancet* (ii), 537.
RAMON, G. (1945) *Pr. Méd.*, 41, 545.

Dr. F. R. Curtis: *Venereal disease control in Denmark, Sweden and the British-occupied Zone of Germany.*—In Denmark and Sweden prior to 1939 there had been a steady fall in the incidence of syphilis and gonorrhœa since 1919-20. In both countries notification of venereal diseases and compulsory treatment had been the law for many years and had become an accepted part of the social fabric. The figures in the table (*v.i.*) can, therefore, be considered reliable.

Between 1939 and 1944 syphilis in Denmark increased almost eightfold, while in Sweden the increase was threefold. The difference may reasonably be attributed to the much greater wartime disturbance of social conditions in Denmark associated with occupation by German troops.

It is also worthy of note that the increase in gonorrhœa in both countries from 1939 was much less than the increase of syphilis, being approximately 2·5 times for Denmark and 1·5 for Sweden.

Both countries emerged from the war convinced that the increased incidence of gonorrhœa and syphilis was but a transient wartime phenomenon and that their well-tried control measures would once more exert their pre-war power as soon as social disturbances subsided.

The British-occupied Zone of Germany presents a very different picture. Here there was no pre-existing system of efficient control of venereal diseases. Little or no use was made of the free public clinic. Practically the only cases treated in hospitals were prostitutes who were sent there by the police, whose responsibility it was to supervise prostitutes and brothels. Naturally a certain number of patients attended the skin and V.D. out-patient departments of the University Hospitals because they were attracted by the prestige of the Professors but could not afford to pay for private treatment.

The local authorities in Germany were under no compulsion to appoint venereologists to supervise the operation of control in their areas, though some states, e.g. Thuringia, took steps to make such appointments with on the whole very favourable results. The fact that so much venereal disease was treated privately made epidemiological work difficult if not impossible for the public health authorities. Nominally there was a professional, but not legal, obligation on every doctor seeing a fresh infection to endeavour to bring the infectious source under treatment. If he failed, he was supposed to furnish particulars to the Medical Officer of Health, who, after failing to achieve success by means of correspondence, could do no more than hand the matter over to the police. To a very large extent the whole system failed to work and except in relation to the regular medical examination of prostitutes it was not surprising to find that the health visitor and social service worker had no place in the scheme of venereal disease control.

The problem of Military Government and then of Control Commission for Germany was first to implement those parts of the German law on venereal disease which were sound but had been somewhat neglected and later to add provisions which would force the local public health authorities to take effective action and at the same time ensure that the British public health officers were able to exercise effective supervision.

During the first year of occupation many parts of the British Zone were inadequately supplied with sulphonamides for all purposes. This led, in the case of gonorrhœa, to a sort of rationing system by which all cases got a little but few got enough. The results in the way of asymptomatic infectiousness and sulphonamide resistance can easily be imagined. The German venereologists admitted that 40% of cases of gonorrhœa were resistant to sulphonamides.

In an endeavour to reduce this reservoir of gonococcal infections as quickly as possible penicillin was obtained from the United Kingdom, since the Germans had never produced penicillin themselves. As they had no experience of penicillin treatment arrangements were made for the leading venereologists to visit the British Army V.D. treatment centres, and they were made responsible for training their colleagues. At the same time, to avoid as far as possible leakage of penicillin to the black market it was made mandatory that cases of gonorrhœa should be treated only in certain specified University or Municipal hospitals.

One of the early preoccupations of public health officers was the possibility of considerable numbers of cases of venereal diseases amongst displaced persons. I made a survey in the summer of 1945, visiting camps containing altogether about 60,000 such persons which represented approximately 10% of the total in the area. From inspection of the case-books at the sick bays in the camps and from detailed talks to the medical personnel in charge it became evident that, though in many instances conditions were highly favourable to the spread of venereal diseases, there was in fact a negligible incidence amongst displaced persons. This was confirmed by numerous UNRRA medical officers not only in the area under survey but also in other parts of the British Zone.

The rates for England and Wales are calculated from Tables A and B on pages 272 and 273 of Report of the Chief Medical Officer of the Ministry of Health, 1939-45.

RATE PER 10,000 OF TOTAL POPULATION

	England and Wales		Denmark		Sweden		Germany (British Zone)
	1939	1944	1939	1944	1939	1944	1946
Gonorrhœa	7·4	6·5	21·8	58·5	19·4	32·0	46·7
Syphilis	2·8	3·8	1·3	10·2	0·7	2·1	19·8

The rates for Denmark and Sweden are obtained from page 33 of Hartmann's "The Girls they Left Behind", Copenhagen, 1946.

The rates for British Zone of Germany are calculated from figures in a paper published in the *British Journal of Venereal Diseases*, 1947, 23, 20.

(1) It must be remembered that the figures given for England and Wales are for attendances at treatment centres only and exclude Services cases as well as gonorrhœa and syphilis treated privately.

(2) The conditions in Germany, owing to the absence of so many men of military age as prisoners of war, approximate to those obtaining in England and Wales in 1944. It is of interest that in both England and Wales and Germany in 1944 and 1946 respectively the incidence of venereal diseases was greater in females than in males as judged by the returns. This occurred for the first time in England and Wales since the records had been kept. It is of course almost certainly related to the preponderance of young women over young men at the relevant times.

(3) The figures for gonorrhœa in Denmark and Sweden are far higher than those in England and Wales. In the former countries notification is the law, whether cases are seen privately or at public clinics. It would be premature to conclude that gonorrhœa is a less common disease in England and Wales than in the Scandinavian countries until appropriate action has been taken to implement the recommendations of the Ministry of Health Medical Advisory Committee that "some form of regular return which would provide information about the number of patients treated by private practitioners should be adopted" (Page 71, Chief Medical Officer's Report on the State of the Public Health during Six Years of War).

(4) The very low ratio of gonorrhœa to syphilis in British Zone of Germany should be compared with the corresponding ratios for Denmark and Sweden.

(5) It is noteworthy that in Denmark and Sweden between 1939 and 1944 there has been an increase in syphilis disproportionate to that in gonorrhœa, and that the disproportion is far greater in Denmark, which was occupied, than in Sweden which was not. If there were any reliable figures available it would probably be evident that the same disproportion occurred in Germany. Certainly the leading German venereologists were convinced of such disproportionate increase in their own spheres of influence.

Dr. J. Balfour Kirk said that the spraying of houses with D.D.T. as a method of malaria control had been advocated by de Meillon and Park Ross in Natal some twelve years ago. Russell and Knipe employed it with conspicuous success in certain villages in India. The method had also been put into effect in Mauritius in 1941 as a means of protecting from malaria a large camp of Jewish immigrants, and also at Takoradi on the Gold Coast in 1942. In those experiments pyrethrins or an extract of pyrethrum made with kerosene oil had been used, as well as dusting with a fresh pyrethrum powder. D.D.T. by itself, owing to its delayed action and to the fact that it was not repellent, was unlikely to be entirely satisfactory in house-spraying. Possibly a more effective mixture would be D.D.T. and pyrethrins.

Dr. Kirk remarked that the danger of a European pandemic of communicable disease arising from localized outbreaks in more backward countries such as those of the Balkans or Eastern Europe, was not really great, because these countries had been largely deprived of means of rapid transport. Although their health departments had been very seriously disorganized, they were probably sufficient to deal with local outbreaks. The danger might arise if rapid international transport were re-established before the various health departments were sufficiently organized to deal with country-wide outbreaks.

The success of the UNRRA Displaced Persons Operation in Germany during the winter of 1945-46 in keeping to remarkably low levels the incidence of communicable disease in the camps Dr. Kirk attributed to the fact that the danger had been adequately anticipated by Military Governments and UNRRA, and that such preventive measures as were practicable had been very thoroughly applied throughout and in good time.

Dr. Milosh Sekulich said that in Jugoslavia to-day, a doctor was never sure of his position in the community unless he was a "party man". There was no question to-day of introducing a new system—a National Medical Service—because national medical service was gradually introduced between the two great wars. Doctors were engaged in this national medical scheme both on a whole-time and part-time basis, the latter being allowed private practice, and thus retaining their identity as "family doctors".

Prior to 1918, Jugoslav doctors were educated abroad, but, from then onwards, three medical schools were created and over three thousand doctors were trained. Over three hundred new institutions were set up for work on preventive medicine, and over three hundred hospitals, clinics and other institutions were opened for curative medicine. As a result of this medical progress in Jugoslavia between the two great wars, the fight against infectious diseases was increasingly successful. Diseases like smallpox were quite unknown in the country, while typhoid, typhus and diphtheria were progressively reduced. The fight was very difficult, and, in spite of all efforts, endemic typhus and syphilis remained virulent in some parts of the country until the present time.

It is interesting to note that the pre-war semi-dictatorships favoured the development of medical service, and many new laws were created to this end. Under the Communist totalitarianism of to-day, medical work was far from being successful in spite of the enormous help given by UNRRA. The Communist Government of Jugoslavia received as a gift from UNRRA the equivalent in value of six years' national budget, yet unfortunately almost daily pathetic letters from that country were received, asking for even a few grains of aspirin.

[*May* 2, 1947]

Common Cold.

Interim Report on a Transmission Experiment. [*Abstract*]

By Doctors C. H. Andrewes, W. H. Bradley, D. K. M. Chalmers and F. Fulton
(*Common Cold Research Unit, Harvard Hospital, Salisbury.*)

THIS meeting was held on May 2, 1947, at the Common Cold Research Unit, Harvard Hospital, Salisbury, where for about a year, under auspices of the Medical Research Council and the Ministry of Health, an investigation into the ætiology of the common cold has been undertaken. Successive groups of volunteers have accepted isolation for ten to fourteen days to be tested with the common cold virus.

Members of the Section and others visited the isolation quarters and later heard a review of the present position of the experiment and saw a film of the Unit which had been produced by the Central Office of Information. Dr. H. J. Parish, the Chairman, pointed out that the common cold was reputed to be responsible for the loss of 40 million man-days per year, but this was the first time the Section had discussed the subject.

At the time of Dunkirk, Harvard University in America sent to this country a number of field and laboratory workers to assist in the control of epidemics. A group of prefabricated buildings formed the hospital at Salisbury and the Harvard Unit grew into a team of more than 100 doctors. The hospital became an E.M.S. hospital for both civil and military cases of communicable diseases. The course of the war prevented the full benefit of the studies from being reaped, but the result of some of the work was published in the reports for the war years of the Chief Medical Officer of the Ministry.

With America's entry into the war the hospital passed into the hands of the U.S. Army and became the central laboratory for the American Army Medical Corps in the European theatre. The laboratories were extended and special research units were established. The place rapidly acquired a reputation as one of the foremost laboratories devoted to preventive medicine. In 1944 the central laboratory was transferred to the Pasteur Institute in Paris. In May 1945 the American military authorities withdrew from the hospital which now remains an important link between the United States and Great Britain on the one hand and between Harvard University and its Faculty of Medicine and the British Ministry of Health and the Medical Research Council on the other.

The hospital was built specifically as an institute for the study of communicable diseases. In 1946 it was decided to adapt it for a long-term research into the ætiology and transmission of the common cold.

The first requirement is to discover a method of studying the virus of the common cold which cannot at present be handled in the laboratory by existing techniques. Human volunteers are therefore employed as indicators of the presence of cold-producing agents, but it is hoped that eventually a substitute will be found for the human volunteers.

It has been known for more than thirty years that a cold can be transmitted from one person to another by means of bacteria-free filtrates, and that such colds are transmissible in series. It is also known that chimpanzees—but no other kind of animal—can also be infected. A claim to have cultivated the virus in a tissue culture medium is not yet confirmed. The most likely working hypothesis is that the filtrable agent which can produce transmissible colds in series is a virus.

The primary objective is to find some substitute for the human volunteer, some laboratory method by which to recognize the presence of the virus. An attempt is being made, first of all, to adapt to the study of the cold a number of virus techniques which have been developed during the last fifteen years. Concentrated attempts are being made to grow the virus in fertile eggs because about sixty different viruses have been studied in this way, and in about 75% success has been obtained by one or other technique. Attempts are being made to grow the agent in the egg and to use human volunteers to decide whether the experiment is getting anywhere. The problem is not one which can be solved quickly.

It has been suggested, particularly by recent work in America, that there might be some infections simulating the common cold but with a much longer incubation period than two or three days. If this is so the technique in use at the research unit is open to serious criticism, but the possibility is recognized. To allow a fortnight or more for long incubation periods would seriously curtail the speed of the research.

Volunteers are isolated on the assumption that they are likely to pick up colds by contact with other people. No stringent precautions are taken to prevent the infective agent reaching the volunteers by means of inanimate objects, such as newspapers and milk bottles: these are not believed to be serious sources of danger. The system of controls is such as to give some indication if these precautions are inadequate. A full-blown cold is not difficult to detect clinically, but there are bound to be many intermediate conditions. To avoid a bias in any trial, certain volunteers receive normal egg fluids or other materials known not to contain cold virus and nobody but the laboratory workers knows what is given to any volunteer. Twenty-four people—12 pairs—are taken at each trial. Two of the pairs receive negative control material and, in most trials, two positive control material. This leaves 8 pairs for the material to be tested. Something like 50% of the people are resistant to the material, so that to test any one material it is necessary to take at least four subjects, two pairs, as a minimum. There must be no disappointment if progress is rather slow. Other angles of approach are possible in the future—a study of the individual resistance of the patient, epidemiological studies, air hygiene, climatology and orthodox bacteriology, but it is felt that orthodox bacteriology has been studied rather more than other aspects.

At the Unit itself, the task is to provide the bacteriologists with human subjects in isolation under such standard conditions as are practicable and then to make the clinical assessment on which to base the result of the experiment. The age limit for volunteers is 18 to 40—after school age and before the setting in of the chronic catarrhal conditions of later life. People with asthma, hay fever, sinusitis, or a history of pulmonary tuberculosis are excluded. There is almost complete freedom for volunteers except that they must not mix with other people. A distance of 30 feet is regarded as beyond the reach of cross-infection. Each trial lasts for ten days. After a communal lunch on arrival, the volunteers are given a preliminary talk, undergo a medical examination of life insurance standard (but including an X-ray examination of the chest and sinuses) and then go into quarantine for seventy-two hours to exclude incubating colds. Materials believed to contain virus or materials known not to contain virus are instilled into the nose, 0·5 ml. into each nostril, with the subject maintaining the supine position for two minutes followed by the prone position for one minute.

Clinical assessment begins on the fourth day of the trial and continues throughout the remainder of the trial. The matron records pulse and temperature daily on a chart. The

criteria of each assessment are subjective and objective. Each volunteer reports any symptoms he or she may have. The appearance of the fauces is noted and especially the evidence of what can be blown out of the nose on to the handkerchief.

It may well be that the experimental cold induced in the Unit is not the same thing clinically as the cold seen outside. For one thing there should be less secondary infection. The induced colds vary from the doubtful abortive cold to abundant rhinitis. The most common incubation period is two to three days, but a few colds develop after five or six days, which is the limit of the period of observation ; therefore the present period of observation is not ideal, although the majority of colds probably exhibit themselves within that time. It does not appear significant whether the subject has had a cold during the previous month or has had no cold for six months.

Material for transmission experiments is collected from suitable subjects, packed in solid CO_2, sent to the laboratory and centrifuged. The filtrate is cleared of all bacteria and then stored. The first problem is to determine whether it is possible to go on storing the material indefinitely and still maintain the life of the virus. It has been shown that the filtrate can be stored for at least four and a half months at −76° C. At ordinary icebox temperature, +4° C., activity persists for at least three days. An attempt is also being made to determine the size of the agent responsible. The washings can contain substances of quite different sizes. It cannot be said that the lower limit of size is fixed; the upper limit is fixed but not the lower. The only thing certain is that there is some agent in the common cold filtrates which induces colds in a percentage of people; all other results are tentative.

Section of Comparative Medicine

President—G. R. CAMERON, F.R.C.P., F.R.S.

[*February* 19, 1947]

Teratomas and Mixed Tumours in Animals and their Bearings on Human Pathology. [*Summary*]

By Professor R. A. WILLIS

THE following distinct kinds of tumours should not be confused with one another: (1) Mixed tumours of adult tissues, e.g. of the breast, thyroid and uterus. (2) Embryonic tumours of particular organs, arising in early life from tissues which are still immature, e.g. embryonic tumours of the kidney, liver, and pelvic viscera. (3) Teratomas, composed of a variety of tissues quite foreign to the parts in which they arise.

Tumours of the first class, e.g. mammary fibro-adenoma, contain both epithelial and non-epithelial neoplastic tissues. By serial transplantations of the mammary tumours of rats, several workers have found that the fibromatous component can be separated from the epithelial component and its properties studied, especially its sarcomatous transformation. Informative results might be obtained by similar transplantation of the common mammary fibro-adenomas of dogs, the fibromatous element of which, besides undergoing sarcomatous change, often ossifies or chondrifies; or by similar studies of the rarer mixed tumours of the dog's thyroid, or of other mixed tumours which may be discovered from time to time in animals.

Tumours of the second class also occur in animals, e.g. embryonic renal tumours, believed to be the counterparts of the human ones, are not uncommon in pigs, rabbits and possibly birds. Analysis of the structure and properties of these by transplantation deserves further study. Such tumours not infrequently show aberrant differentiation of their tissues in part.

Teratomas appear, with one exception, to be very rare in animals. The exception is the benign type of teratoma which occurs frequently in the testes of young horses. (Several examples of these were shown to the meeting.) It is a striking fact that, while dogs frequently develop seminomas, interstitial-cell tumours and Sertoli-cell tumours, teratoma of the canine testis has not been described. Ovarian teratomas are very rare in dogs, and also in rodents. But there is great need of analysis of the properties of the various components of these growths by serial transplantation.

criteria of each assessment are subjective and objective. Each volunteer reports any symptoms he or she may have. The appearance of the fauces is noted and especially the evidence of what can be blown out of the nose on to the handkerchief.

It may well be that the experimental cold induced in the Unit is not the same thing clinically as the cold seen outside. For one thing there should be less secondary infection. The induced colds vary from the doubtful abortive cold to abundant rhinitis. The most common incubation period is two to three days, but a few colds develop after five or six days, which is the limit of the period of observation; therefore the present period of observation is not ideal, although the majority of colds probably exhibit themselves within that time. It does not appear significant whether the subject has had a cold during the previous month or has had no cold for six months.

Material for transmission experiments is collected from suitable subjects, packed in solid CO_2, sent to the laboratory and centrifuged. The filtrate is cleared of all bacteria and then stored. The first problem is to determine whether it is possible to go on storing the material indefinitely and still maintain the life of the virus. It has been shown that the filtrate can be stored for at least four and a half months at −76° C. At ordinary icebox temperature, +4° C., activity persists for at least three days. An attempt is also being made to determine the size of the agent responsible. The washings can contain substances of quite different sizes. It cannot be said that the lower limit of size is fixed; the upper limit is fixed but not the lower. The only thing certain is that there is some agent in the common cold filtrates which induces colds in a percentage of people; all other results are tentative.

Section of Comparative Medicine

President—G. R. CAMERON, F.R.C.P., F.R.S.

[*February* 19, 1947]

Teratomas and Mixed Tumours in Animals and their Bearings on Human Pathology. [*Summary*]

By Professor R. A. WILLIS

THE following distinct kinds of tumours should not be confused with one another: (1) Mixed tumours of adult tissues, e.g. of the breast, thyroid and uterus. (2) Embryonic tumours of particular organs, arising in early life from tissues which are still immature, e.g. embryonic tumours of the kidney, liver, and pelvic viscera. (3) Teratomas, composed of a variety of tissues quite foreign to the parts in which they arise.

Tumours of the first class, e.g. mammary fibro-adenoma, contain both epithelial and non-epithelial neoplastic tissues. By serial transplantations of the mammary tumours of rats, several workers have found that the fibromatous component can be separated from the epithelial component and its properties studied, especially its sarcomatous transformation. Informative results might be obtained by similar transplantation of the common mammary fibro-adenomas of dogs, the fibromatous element of which, besides undergoing sarcomatous change, often ossifies or chondrifies; or by similar studies of the rarer mixed tumours of the dog's thyroid, or of other mixed tumours which may be discovered from time to time in animals.

Tumours of the second class also occur in animals, e.g. embryonic renal tumours, believed to be the counterparts of the human ones, are not uncommon in pigs, rabbits and possibly birds. Analysis of the structure and properties of these by transplantation deserves further study. Such tumours not infrequently show aberrant differentiation of their tissues in part.

Teratomas appear, with one exception, to be very rare in animals. The exception is the benign type of teratoma which occurs frequently in the testes of young horses. (Several examples of these were shown to the meeting.) It is a striking fact that, while dogs frequently develop seminomas, interstitial-cell tumours and Sertoli-cell tumours, teratoma of the canine testis has not been described. Ovarian teratomas are very rare in dogs, and also in rodents. But there is great need of analysis of the properties of the various components of these growths by serial transplantation.

criteria of each assessment are subjective and objective. Each volunteer reports any symptoms he or she may have. The appearance of the fauces is noted and especially the evidence of what can be blown out of the nose on to the handkerchief.

It may well be that the experimental cold induced in the Unit is not the same thing clinically as the cold seen outside. For one thing there should be less secondary infection. The induced colds vary from the doubtful abortive cold to abundant rhinitis. The most common incubation period is two to three days, but a few colds develop after five or six days, which is the limit of the period of observation; therefore the present period of observation is not ideal, although the majority of colds probably exhibit themselves within that time. It does not appear significant whether the subject has had a cold during the previous month or has had no cold for six months.

Material for transmission experiments is collected from suitable subjects, packed in solid CO_2, sent to the laboratory and centrifuged. The filtrate is cleared of all bacteria and then stored. The first problem is to determine whether it is possible to go on storing the material indefinitely and still maintain the life of the virus. It has been shown that the filtrate can be stored for at least four and a half months at −76° C. At ordinary icebox temperature, +4° C., activity persists for at least three days. An attempt is also being made to determine the size of the agent responsible. The washings can contain substances of quite different sizes. It cannot be said that the lower limit of size is fixed; the upper limit is fixed but not the lower. The only thing certain is that there is some agent in the common cold filtrates which induces colds in a percentage of people; all other results are tentative.

in both sexes at birth, but are best developed after puberty. They form a ring around the anus, but are most numerous above it; tumours of these glands are most often seen above the anus, but they may occur anywhere around the anus, or even at the base of the tail or the side of the prepuce. The tumours do not form metastases, but they have a vascular stroma and are liable to bleed, and their position exposes them to infection.

Tumours of the circumanal glands occur almost exclusively in males, and Smythe (1945, 1946) has introduced a method of treatment with stilbœstrol which often has satisfactory results; these are, however, sometimes only temporary. The circumanal gland tumour occurs in old dogs, and it is possible that it should not be classed as a neoplasm, but as an example of those hyperplasias of endocrine origin which occur in old dogs, such as hyperplasia of the interstitial cells of the testis or hyperplasia of the prostate.

(3) *Mammary tumours of the bitch.*—This is the commonest tumour we are asked to examine—110 of the 550 tumours mentioned were from the mammary gland. The tumours usually occur in older animals, are often well encapsulated, and may be multiple. They tend to be more frequent in the posterior pairs of mammary glands, and usually grow slowly and intermittently over months or even years.

At least one-third of the 110 tumours were of the mixed type, showing, in addition to the epithelial component, myxomatous fibrous tissue, cartilage, pseudocartilage, and sometimes bone. The cartilage and bone are apparently formed by metaplasia of the stromal connective tissue, and the pseudocartilage by the appearance of interstitial matrix between the epithelial cells. Some have claimed that the pseudocartilage is true cartilage of epithelial origin; for example, Allen (1940) found the material to have the staining and biochemical properties of cartilage, and he considers that the absence of a perichondrium around the pseudocartilage is not evidence of its non-cartilaginous nature, but is merely what would be expected if it was, in fact, of epithelial origin. The myxomatous and other changes appear to affect mainly the intralobular as opposed to the interlobular tissue, and a study of the changes in this tissue during the normal sexual cycle might provide a clue to the significance of the structure of the tumour.

An attempt has been made to assess the nature of 69 tumours from their histological structure: 29 were thought to be certainly benign, and 9 probably so; 10 were thought to be malignant, and 10 probably so; the nature of 11 was doubtful. These figures are probably misleading as to the actual proportion of benign to malignant cases that might be encountered in practice, partly because clinically quite benign tumours may show a disordered histological structure suggesting malignancy. Dobberstein and Matthias (1942) consider that not more than 10% of the mammary tumours of the bitch are truly malignant as shown by the production of metastases, and they show that many of the descriptions of malignant tumours in the literature were based on insufficient evidence of malignancy or of mammary origin.

With regard to the possible ætiology of the mammary tumours of the bitch, they seem to be commoner in those bitches that have bred infrequently or not at all—this recalls the incidence of "pyometra" in the bitch, which is possibly due to a hormone imbalance provoked or accentuated by repeated pseudo-pregnancies. It is possible that retention of milk may account for the more common occurrence of the tumours in the posterior glands, as they are larger and have larger teats and may not be so thoroughly milked out by the pups even when true pregnancy has occurred. Huggins and Moulder (1944) found that the mammary glands of the bitch undergo regional involution, some degree of functional activity often being retained longer in the posterior than in the anterior glands.

One case of what appeared to be a typical mixed mammary tumour was seen in a male dog, and others have been recorded.

The only instance of such a study in a mammal appears to be that of Jackson and Brues who examined the growth of a malignant ovarian teratoma of a mouse through 13 generations of transplants.

REFERENCE

JACKSON, E. B., and BRUES, A. M. (1941) *Cancer Res.*, 1, 494.

Dr. C. L. Oakley showed reconstructions of slices of a teratoma of ovary of a young bitch.

Dr. L. Foulds referred to difficulties in the experimental analysis of mixed tumours. If transplantation succeeded it was probable that even if multiple neoplastic components were present, one would outgrow the others. Primarily simple tumours, however, were observed to become complex during the course of serial transplantation as a result of changes induced by the parenchyma in the stroma or invaded tissues. Dr. Foulds agreed with Professor Willis in placing the teratomata in a group by themselves but thought that the majority of so-called "mixed" tumours were primarily simple tumours with one neoplastic component which had become complex as a result of secondary changes in the stroma or invaded tissues. There was good experimental evidence for the sarcomatous transformation of the stroma in the course of transplantation of mammary carcinomata in mice. At one stage the tumours appeared to be mixtures of sarcoma and carcinoma but subsequently the carcinoma was eliminated and the tumour was then transplantable as a pure sarcoma.

Some Glandular Tumours of the Dog

By E. COTCHIN, M.R.C.V.S.

(1) *The "sweat gland adenoma".*—Visible sweating in dogs is generally confined to the pads of the feet, but this is not due to the absence of glands resembling sweat glands from the general body surface. The dog's sweat glands, unlike those of man, open, except on the pads, into hair follicles and not on to the skin surface (Speed, 1941) and do not normally produce visible sweat; they resemble the apocrine glands in structure.

A few well-defined tumours of the skin of dogs have been encountered which are thought to be of sweat gland origin. They are encapsulated, may be lobulated, and may ulcerate. They consist of epithelial cells resembling basal cells lying in spaces in a fibrous stroma and tending to form long rope-like columns and structures resembling starfish in shape. The latter, which appear to be nodes from which the cell columns radiate, are seen in some other skin tumours, and are composed of a peripheral layer of cells tending to lie at right angles to the stroma and of a central mass of spindle-shaped cells. The cell columns are from one to two cells thick, the cells lying at right angles to the length of the column, and there is no lumen. The arrangement of the cells in the columns, and the relation of the columns to the stroma, are those seen in a developing sweat gland before it has formed a lumen. The name "basal-cell carcinoma" sometimes applied to these tumours is misleading, as, despite the presence of mitoses and the apparently invasive nature of the growth of the cell columns in the stroma within the limits of the tumour capsule, they are not malignant.

(2) *The "anal adenoma".*—This tumour was seen 30 times in a series of 550 dog tumours examined. There are several kinds of glands in the anal region of the dog—the internal anal glands at the junction of rectal mucosa and anal canal epithelium, the glands in the walls of the anal sacs, the local sebaceous and sweat glands, and finally the circumanal glands from which the anal adenoma develops. These circumanal glands are modified sebaceous glands of unknown function. They consist of solid alveolar masses, their ducts usually opening into hair follicles. The alveoli consist of small darkly-staining peripheral cells, and large cytoplasm-rich central cells; in sections, the latter often appear to be separated by canaliculi, and from their supposed method of secretion they have been called "hepatoid glands" by Schaffer (Bolk *et al.*, 1939). The circumanal glands occur only in canines. They are present

It has been demonstrated experimentally for the moth *Tineola biselliella* by E. Titschack, that the greater the body length the greater the span of life. It is probably true generally both for the vegetable and animal kingdoms that in broad terms the longest lived are the large organisms whereas small organisms are generally short-lived. It has been stated that for organisms of comparable size aquatic animals exhibit greater longevity than terrestrial ones, which, if true, may not be without significance. But in connexion with size we may note that the potentially immortal organisms are usually minute but inhabit a liquid environment, a point to which we must revert later. In the small terrestrial organisms a high rate of metabolism is usually a necessary concomitant of the large ratio of surface to volume. In the fruit fly, the span of life has been shown to vary directly with the body weight, and inversely as the rate of metabolism.

Let us consider those plants in which the span of life normally appears quite definite, namely the annuals, which complete their life-cycle in anything from a few months to just over a year. We know experimentally that at least some of these can have their life artificially prolonged by preventing them flowering and fruiting. Indeed, so slender an annual as the sandwort can become perennial under natural conditions which preclude normal reproduction. Here it would appear that the brevity of life is linked with its gaiety and that exhaustion of food resources plays a large part in rendering the organism susceptible to the immediate causes of death. But continuing the analogy of the machine, reproduction is I think only to be regarded as an additional strain, sometimes severe, but that it is far from being the main cause of the limitation of the span of life is shown by the fact that some exotics which we grow here, which do not flower or fruit, though they appear to flourish vegetatively, are not in any degree remarkable for an increased span of life.

No, the secret lies deeper and I think we can come nearer the heart of the problem by considering a few concrete examples. Many species of *Dianthus*, as every gardener is aware, are short-lived perennials. Yet if we take cuttings from the periphery of the plant we can, by repeating the process, prolong the life of the individual apparently indefinitely. Varieties of sugar-cane are propagated by means of the top joints only and Bourbon for instance has been in cultivation for two hundred years or more without loss of vigour. It would appear then as if removal of the younger from continuity with the older parts of the plant had a rejuvenating effect. In the pseudo-annual herbs such as the Enchanter's Nightshade, the same effect is produced by the rapid decay of the older parts at the end of each season. The cultivated potato behaves as a pseudo-annual and except for the greater incidence of virus disease the potato shows no loss of vigour. The prevalence of virus diseases might be regarded as a sign of diminishing vigour in the stock were it not that this is probably not an outcome of changed susceptibility but rather of the vastly augmented opportunities for infection. The giant trees in California are known to attain an age of over 2,000 and possibly 5,000 years, but it must be remembered that the tree develops new living tissue on the outside of the old each year, whilst the heart wood dies from within outwards. Thus no part of the tree actually remains alive for centuries though individual cells may perhaps persist for nearly one hundred years. The anything but robust mycelium of the fairy ring fungus could with equal justice be claimed to attain to a great age, for such rings are known from the downs which from their diameter must be at least 400 years old, but here, as with the tree, a new living zone is added on the outside as the mycelium within dies and decays. Despite this juvenile tissue added without, a common feature of nearly all trees, we find that each species has its normal span of life; this, though subject to variation with the conditions of growth, is a feature that has been shown to depend in part at least on genetic factors.

Let us now turn to the unicellular plants for which it has been claimed that they are potentially immortal. If, for instance, we study the life-cycle of such aquatic plants as the unicellular Chlamydomonads, we find that each individual is capable of growth and division and that the entire living substance of the parent is embodied in that of its vegetatively produced offspring. The same is true of the bacteria, of yeasts, and of many others. In one sense then we can speak of these as potentially immortal organisms. The essential difference here is that the entire substance appears to be potentially immortal whereas in the Dianthus potential immortality is characteristic only of a part, though an appreciable part, of the organism and it is relevant to note that the much more academic concept of potential immortality in the sex cells of sexually produced offspring embodies but a microscopic part of the living material of each successive parent and this, moreover, may undergo change in kind.

It would appear then that continuity of life, except in the unicellular organisms referred to, is dependent upon separation of the newly-formed parts from the old.

Some twenty years ago I called attention to the fact that the root systems of flowering plants could be strikingly checked in their growth by the presence of the root systems of other species. Subsequently, Varma working in my laboratory was able to show that this was due to water soluble substances and there is evidence that though such substances may be important as weapons in the competitive struggle, unless removed they are deleterious also to the producing organisms.

Such antibiotics are now familiar from the special example of penicillin. For our present purpose their significance is the evidence it affords of the production by the living organism, as a by-product

REFERENCES

ALLEN, A. C. (1940) *Arch. Path.*, 29, 589.
BOLK *et al.* (1939) Handb. vergleich. Anat. Wirbeltiere. Berlin and Vienna, 1, 665.
DOBBERSTEIN, J., and MATTHIAS, D. (1942) *Arch. wiss. prakt. Tierheilk.*, 78, 18.
HUGGINS, C., and MOULDER, P. V. (1944) *J. exp. Med.*, 80, 441.
SMYTHE, R. H. (1945) *Vet. Rec.*, 57, 115; (1946) *Vet. Rec.*, 58, 75.
SPEED, J. G. (1941) *Vet. J.*, 97, 252.

Miss J. O. Joshua: Clinically the anal tumours described by Mr. Cotchin are invariably benign: they occur in a variety of forms, from single circumscribed masses to diffuse involvement of the entire anal rim. This rather supports the suggestion that the condition is a hyperplasia and not neoplasia, as also does the fact that, prior to the introduction of stilbœstrol therapy, treatment of these tumours by simple expression of the contents followed by cauterization of the cavity was successful. An interesting point in connexion with stilbœstrol treatment is that in addition to regression of the tumours there is almost invariably improvement in the general health of the dog, in spite of the fact that the owner has not as a rule complained of general symptoms shown by the dog prior to the initiation of treatment.

The condition occurs in dogs over middle age, in most cases household pets which have had little or no sexual activity; one case had occurred in a popular stud dog which had been overworked during his breeding life; both might, however, be attributed to hormonal disturbance.

With regard to mammary neoplasms in bitches, these again usually occur in bitches which have not bred. in fact I can recall only one case of mammary neoplasia in a bitch which has been regularly bred. The phase of most rapid growth of these neoplasms nearly always coincides with the period of pseudo-lactation following œstrus. Frequently small nodules of tumour tissue have been present for a long period before active enlargement occurs. It is inadvisable to undertake surgical interference during the period of pseudo-pregnancy.

In the small percentage of cases in which there are malignant changes metastasis has often occurred not via the lymph nodes, but direct to the lungs, where multiple highly malignant tumours have developed resulting in rapid death of the patient.

Mrs. M. Mandeville and **Professor A. Haddow** read a paper on "Melanoma Occurring in the Viviparous Fish *Heterandria formosa*, and associated with Sex Reversal".

[*March* 19, 1947]

DISCUSSION ON THE SPAN OF LIFE

Sir Edward J. Salisbury: The problem of the span of life is of both economic importance and great scientific significance. But in this connexion the question immediately arises: Why do organisms die? For those who think of a plant merely as a mechanism concerned with the business of living the analogy with a machine that gradually becomes less efficient with age and is liable to succumb to a variety of causes that add to the strain upon the mechanism is familiar. If the immediate cause of the death of a tree be its uprooting in a storm or its destruction by diseases or pests, it is nevertheless a fact that the saplings commonly survive these trials whereas the old trees perish. If accidents be the immediate cause, impaired vitality is the more remote one.

If we employ the usual, and may I add rather equivocal, meaning which attaches to the phrase "span of life" it is true to say that the maximum longevity of certain plants far exceeds that of the longest lived animals. For example, the Mexican Swamp Cypress that attains perhaps two millenia, or the famous Sequoia Giganteas of California that perhaps attain to over four millenia, are of a different order of life span to that of a fish, such as the famous Pike of Kaiserslautern, which is alleged to have attained an age of 267 years, or of an elephant, or even a tortoise which may attain to over 200 years. But, in fact, we are in reality comparing different things because the tissues of the old animal occupy the same position in space as those of the young, a condition essential to a mobile organism that would be handicapped by an ever-increasing bulk, whereas in the plant there is no such in situ renewal but a juxtaposition of juvenile tissue. Though span of life in a higher animal means something different from that of a higher plant, it will I think be true to say that the distinction is a concomitant of the high degree of differentiation of advanced members of the two kingdoms, the sedentary and mobile habits impose a different type of longevity on each.

for far longer than similar seeds stored in packets in a cupboard, where the metabolic activity is almost certainly greater.

The fact that worker bees during the active season live only four or five weeks compared with up to ten weeks in the inactive season might be held to support the view that the mechanism of living deteriorates with use, but since the rate of production of by-products will increase *pari passu* with the augmented activity this is no more inconsistent with the view here adopted than the well-established diminution in life span with increased temperature that accelerates chemical processes.

Breeding experiments have shown that the span of life is in part at least a genetic phenomenon, but it may well be that this is but an expression of heritable differences in susceptibility to the hypothetical chemical causes of senescence.

Probably no botanical material has been more studied in relation to problems of senescence than detached apples and it is significant to note that one of the two most important factors for the prolongation of the life of apples is checking the rate of metabolism of the living tissues by lowering the temperature and increasing the CO_2 content of the surrounding atmosphere, as in gas storage, both of which may reasonably be assumed to reduce the rate of production of by-products of metabolism. Again, greater longevity can be induced by removal of these same metabolic by-products especially ethylene gas and it is noteworthy that treatment of unripe fruit with even minute traces of this same ethylene collected from ripe fruit will quickly induce symptoms of maturity and old age in the immature apples. It is moreover pertinent to recall that chemical treatment has been known to produce rejuvenation and the use of HCN on Planarians has successfully "put back the clock" again and again with respect to the same individual.

It is suggested that the facts so far known are all consistent with the conception postulated. If the concept be true then the investigation of such by-products, their isolation and the determination of their chemical characteristics, might lead to methods of their neutralization and destruction, to the prolongation of life and perhaps even to the prophet's dream of a millennium when "there shall be no more death" with consequences as fraught with potentialities and dangers as great as those of the atomic bomb.

Dr. John Hammond (*School of Agriculture, Cambridge*): In the higher animals the curve of life begins with a period of growth and development which is followed by one of completed development—the prime of life—and lastly by one of senescence in which the powers of the different functions gradually fail ending in the death of the individual.

Superimposed on this curve of life of the individual as a whole are curves of life of the different individual tissues and organs. An organ such as the mammary gland may have several curves of life during the life of the individual animal (fig. 1). The course of these is influenced by the stage of life of the animal as a whole. In young animals the milk yield does not rise to a high level (due to competition with other tissues for growth substances), but persists for a long time (due to the youth of the animal's tissues). In the prime of life the milk yield rises to a higher level but falls more quickly, while in the downward curve of life the fall off in yield after the maximum is rapid. The various organs and tissues of the body develop in a definite order and it would appear that in the senescence of the individual the first tissues, organs and functions to develop are the last to go.

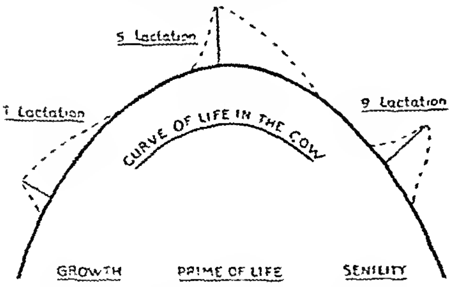


FIG. 1.—Curves of life in the mammary gland.

The duration of life in the various races of animals is very variable and whereas some species are remarkably long lived others die after a relatively brief existence. A sea anemone, belonging to the species *Actinia mesembryantha*, is known to have lived for sixty-six years. Among insects there is an extraordinary variability in the duration of life, some living in a condition of maturity for only a few hours while certain *Hemiptera* are believed to survive for as many as seventeen years. The duration of life is sometimes very different in the two sexes, the queen ant being known to live in some instances for fifteen years whereas the male ant survives for only a few weeks. Reptiles have always been noted for their longevity, a tortoise from the Galopagos Islands being stated to have lived for 175 years. Here long life is associated with a slow rate of living.

of its normal metabolism, of substances which are suppressive of biological activity. Is it on such similar substances that the loss of potential immortality depends? In other words is senescence in plants a condition of increasing auto-intoxication? The effects of increasing temperature in diminishing life span may well be the consequence of more rapid production of by-products relative to their rate of removal.

The fact that many unicellular organisms appear to be potentially immortal may well be due to their large surface in relation to their volume, the liquid media in which they live and in which they move freely.

The well-known experiments of Woodruff on *Paramœcium caudatum*, which he cultivated for 8,000 generations, showed that there was no apparent degeneration or signs of senescence provided that the organisms were continually transferred to fresh nutrient media. Investigations using other organisms have pointed to the same conclusion.

The death which ensues in algal cultures when the medium is unchanged, despite the addition of nutrients, suggests that the senescence is here due to the accumulation of metabolic products which in terrestrial and sedentary organisms must to a greater or less degree accumulate in the body of the organism itself. Is it not possible that the proximal diffusion of such substances away from the actively growing regions of the higher plant leads to an inhibiting accumulation in the older parts of the plant body and thus sows the seeds of ultimate dissolution. The likelihood of such accumulation will depend upon the possibilities for diffusion into the surrounding medium which will be greatest in an aquatic organism of small size whilst for terrestrial plants the contact which the organism makes with the soil may well be a factor. The large increase in such surface of contact of the root system of a higher plant with the soil which is the result of the root hairs may well have a very important significance in relation to water supply when the latter is deficient but abundant root hairs are quite common in species which normally occupy habitats where the absorbing surface is rarely if ever the limiting factor in water supply. It is not improbable that the extended surface of contact provided by the root hairs may have a value in accelerating the removal of toxic products of metabolism and we have, in fact, evidence that water-soluble antibiotics do diffuse outwards in this way. If this were true the trees which should have the greatest longevity would be those with the most extensive root systems penetrating to the levels not densely exploited by the root systems of other species. Whether this is true we have I think no data to test. All we can say is that Nobbe found the areas of the roots in relation to the tops of young trees to be 2 : 1 for Silver Fir, 3 : 1 for Spruce and 5 : 1 for Scots Pine. If similar ratios obtain in the adult trees then the extent of the roots in relation to the living bulk of the trees would seem to correspond roughly to the ages which these species normally attain.

Senescence has by some been held to be a necessary concomitant of differentiation. But though it may well be true that certain types of cell specialization are inconsistent with marked longevity the basis of the wider application of the concept is probably not unconnected with the mistaken view that the potentially immortal types of unicellular organism, because they are morphologically simple are therefore simple in their internal organization and physiology. Indeed, as we know in human mechanisms, the apparently simple is often the most highly differentiated. Moreover it is relevant to note that tissue cultures of meristematic cells are safeguarded against senescence and death only so long as we remove the products of their metabolic activities by renewal of the culture medium. If differentiation retards the rate of such removal it will manifestly become a contributory factor to limitation of the span of life.

Ingle found that the length of life of *Daphnia* could be appreciably increased by dilution of the nutrient medium. Was this because the growth rate was diminished or because removal of by-products was facilitated? On the other hand the span of life of snails has been found to decrease with the number of individuals per unit volume, a fact most readily accounted for by the higher concentration of waste products in the denser populations. The beneficial effects of larger body size are probably due to a similar cause. Again, the persistence of normally short-lived perennials from which the older portions are continually removed may be because in this way the younger portions are protected from the diffusion outwards of the by-products of metabolism that have accumulated in the older plant body.

Again we may recall that many seeds both small and large are known to retain their viability for many years and I have elsewhere furnished evidence that the small seeds of the Pimpernel, which is an annual plant, can retain their viability for more than a century. If we think in terms of the crude machine concept, this does not surprise us for the mechanism that is not working does not wear out; but, equally, it may be that in the absence of active growth there is no production of toxic by-products causing senescence. But that even dormant seeds undergo change is shown not only by their loss of viability with time, but also by the fact that has been demonstrated for a variety of species such as the Antirrhinum, Maize, Barley and Crepis, that there is increased mutation which the ageing of the seed induces. It is noteworthy that seeds under turf which are probably subjected to but slight changes of temperature and an atmosphere of relatively high CO_2 content remain viable

REFERENCES

Brody, S. (1945) Bioenergetics and Growth. New York.

Cannon, C. Y., and Hansen, E. N. (1939) Expectation of Life in Dairy Cows, *J. Dairy Sci.*, 22, 1025.

Harvey, Dr. (1700) Anatomical Account of Thomas Parr, *Philos. Trans.*, 3, 306.

Hunter-Smith, J. (1933) Changes and Events in a Large Dairy Herd from 1912 to 1932, *Emp. J. Exp. Agric.*, 2, 139.

Kelly, R. B. (1939) Female Aspects of Relative Fertility in Sheep, *Aust. vet. J.*, 15, 184.

McCay, C. M., Maynard, L. A., Sperling, G., and Barnes, L. L. (1939) Retarded Growth, Life Span, Ultimate Body Size and Age Changes in the Albino Rat after Feeding Diets Restricted in Calories, *J. Nutrition*, 18, 1.

McMeekan, C. P. (1940-41) Growth and Development in the Pig with Special Reference to Carcase Quality Characters, *J. agric. Sci.*, 30, 276, 387, 511; 31, 1.

Pearl, R. (1938) The Search for Longevity, *Sci. Monthly*, 46, 462.

——, and Raenkham, T. (1932) Studies in Human Longevity. V. Constitutional Factors in Mortality at Advanced Ages, *Hum. Biol.*, 4, 80.

Wallace. L. R. (1948) The Growth of Lambs Before and After Birth in Relation to the Level of Nutrition, *J. agric. Sci.* (in press).

Waller, H. (1939) Clinical Studies in Lactation. London.

Wright, N. C. (1933) Wastage in Dairy Cows, *Scot. J. Agric.*, 16, Jan.

Dr. V. Korenchevsky (*Gerontological Research Unit, Oxford*) discussed the longest span of human life as judged from the records on centenarians in England and Wales. Only the latest data, presumably more reliable, were taken for a period 1930–1945, and subdivided by Dr. Korenchevsky into two sub-periods of eight years each, namely 1930–37 and 1938–45.

These data were obtained from the most reliable source available, the Registrar-General's Statistical Reviews for England and Wales; or, for the latest years, as a personal communication from the Registrar-General's Office at Somerset House, London.

The following conclusions could be drawn from the examination of these data:

(1) In the data recorded in the Registrar-General's Office the certificates of birth of centenarians have not been checked, and therefore their age can be accepted only with some reservation.

(2) According to these data, in England and Wales, per twenty millions of male or female population there were each year on the average 17·7 male centenarians and 71·4 women in the period 1930-1937, and 18·3 men and 83·4 women the latest period of 1938-1945. Their incidence was more or less regular, more women having a long span of life than men. There was a statistically significant increase of female centenarians during the last eight years as compared with a previous period of eight years, whilst a small increase in male centenarians in the last period was not significant.

(3) During these periods the longest human lives were recorded as 109-112 years, which accord approximately with the conclusions reached by previous critical investigators of the span of human life in the periods earlier than 1930. Thus, *theoretically and potentially*, a span of life of 109-112 appears to be possible for every human being. Since, however, the exceptional cases of longevity of human beings have occurred during the present time, when the process of ageing is abnormal, there is some possibility that the span of human life might be further extended, when the process of ageing becomes a normal one.

(4) There are some indications that the genetic factor is one of the causal factors of longevity.

(5) Taking into consideration the primary aim of gerontology to make old age stronger and healthier, not only longer, the prophecy of Professors E. Metchnikoff and I. Fisher may be right, that in this way the useful period of human life might be extended, and there will thus be a greater utilization of the accumulated experience and wisdom of older people for the community.

The detailed paper on the subject will be published elsewhere.

Dr. Muriel Robertson (*Lister Institute of Preventive Medicine*): In English law I believe you cannot be indicted for murder unless the corpse can be produced. I am in much the same case in the matter of the span of life in the Protozoa. If the span of life is concluded, there should remain a corpse, however small. But the Protozoa do not behave like that.

Take for example the flagellate *Heteromita*. It divides by fission with no corpse left. When A becomes A_1 and A_2, there is no end to the span of life. It may be said that these are low simple creatures. In another more developed organism called *Polytoma* there is a process of conjugation: two flagellates fuse and become one. They are haploid organisms and require no reduction divisions to be ready to conjugate. Only the conjugation cyst has the diploid number of chromosomes. At

In birds the length of life varies considerably in different species but the more usual duration of life is from 15 to 20 years. With mammals the length of life in general is longer in the larger species than in the smaller. In domestic mammals large numbers of individual cases of long life have been reported by letters to various papers: horses, in rare cases, have reached over 40 years, cattle somewhat over 30 and sheep over 20 years. Few domestic animals, however, die of old age: Hunter-Smith (1933) found, for example, that in a dairy herd only 5% of the cows survived up to an age of 13 to 16 years, while Wright (1933) and others have shown that old age accounts for only about 4·5% of the wastage of cows from dairy herds. Cannon and Hansen (1939) in U.S.A. found too that only 0·26% of dairy cows reach an age of 15 years or over. The average life of the dairy cow is only about 5 years, although the maximum milk yield is not reached until about the 7th year. Kelly (1939) from the records of a large Merino flock found that 60% survived up to 6 years, 30% to 10 years and 10% to 12 years old.

By retarding growth by nutritional control, that is, by prolonging the upward growth period of the curve of life, McCay *et al.* (1939) were able to increase the mean age of death in rats: members of groups retarded in growth for periods of 100–1,000 days were still alive when the last of the control groups had died at the age of 965 days. Thus physiological and anatomical age can be partially divorced from chronological age. In mammals in general the span of life is prolonged when the length of the growth period is increased, as in the larger animals, and in man who is distinguished from the other animals by the relatively long prepubertal period.

In man a few cases of very long life, such as that of Thomas Parr who lived for 152 years (Harvey, 1700), have been reported but the limit is normally about 112 years. Women, on the average, live to be somewhat older than men. Under modern civilization the chances of life have been increased, but this has been brought about largely by decrease in mortality in early life rather than by increasing the total span of life. For example, Pearl (1938) has shown that in U.S.A., whereas in 1890 56% of males born lived to 40 years of age, in the 1930s 81·6% reached that age; the duration of life after 40 years was, however, but slightly longer than it was in 1890. Similar statistics concerning the numbers per 1,000 births which survive to different ages are very much needed for our domestic animals in order that we can see clearly when, and through which causes, the losses are occurring. These, if taken after definite intervals of time, or under different circumstances of management, would show the effect of these on the life span. For example, Pearl and Raenkham (1932) have estimated that while in ancient Rome the average life expectancy at birth was 25 years, in Rome of the 1930s it was 55 years, while in U.S.A. at that time it was 64 years. The decline in the death-rate in early life, however, is unevenly distributed and the mortality is still high during the first two months, a fact which Waller (1939) attributes largely to defects in the mother's milk supply. This is also true in farm animals and Wallace (1948) has shown that in sheep both the vigour and weight of the lamb at birth and the mother's milk supply can be increased by good nutrition of the mother for eight weeks before parturition.

The steps taken in recent years to control infectious diseases which were formerly the major causes of death in man have now shifted the major causes to those from the insidiously developing degenerative diseases (Brody, 1945). This focuses attention on the order of development and senescence in the different tissues mentioned earlier. This control of infectious diseases and reduction of death-rate from these causes has influenced the age distribution of the population in U.S.A.; thus, while in 1850 some 83% of the population were under 40 years of age, by 1980 only 52% will be under this age. Such comparisons may also be made in space between Eastern and Western peoples. In domestic animals the control of infectious diseases would also do much to prolong the average life-span.

Let us now consider the conditions which affect the normal life-span rather than those affecting the chances of life at birth. Experimental studies on life duration and comparisons between species, as well as analyses of human statistics (much needed in domestic animals), suggest the generalization that the length of life is usually in inverse proportion to the rate of living (Pearl, 1938). In man investigations point to the fact that the main consideration which determines long life is a genetic one. Oliver Wendell Holmes' advice on this point was to select long-lived parents, and particularly long-lived mothers. The average physical characteristics of long-lived and short-lived groups of men show that the former are less of the short thickset type than the latter. These two types can be produced in pigs by control of the nutritional plane during the phase of growth (McMeekan, 1940), high nutrition in the early stages followed by rationing later giving a long, lean animal, while poor nutrition in the early stages (leading to a poorly developed skeleton) followed by high nutrition later giving a short animal with a large accumulation of fat. The accumulation of storage substances and products of metabolism in the body may lead to speedy senescence. Short-lived individuals display a relatively deficient early growth but rapid and unstable accretions of connective tissue elements in late life. Such accumulations are characteristic of old age and their presence throws a strain on the metabolism of the living cellular elements which support these accretions, and consequently tend to shorten life.

Section of Surgery

President—Ernest Finch, M.D., M.S., F.R.C.S.

[*February* 5, 1947]

DISCUSSION ON TREATMENT OF NON-TUBERCULOUS EMPYEMA

Mr. R. C. Brock: *The treatment of acute empyema.*—This is such a big subject that it is not possible in a short introductory talk to do more than discuss briefly a few features. I have therefore chosen for consideration what I think are fundamentals.

(1) *What is an empyema?*—The very wide ignorance of what constitutes an empyema and the looseness of thought and definition that result are the chief cause of many of the differences of opinion expressed about treatment.

An empyema should be defined as a localized collection of pus in the pleura; it is a mature abscess, the end-result of an acute suppurative process. In the early stages there is an acute pleurisy that proceeds to sero-purulent effusion; this sero-purulent effusion matures, the pus thickens, thickened pleural exudate and limiting adhesions develop (unless the empyema is total) until finally an abscess is formed. In the earlier formative stages the sero-purulent fluid is thin and if left in a container will sediment out to give a layer of clear supernatant serous fluid above a deposit of pus. As the process matures the proportion of purulent deposit increases until finally there is little or no supernatant clear fluid. To describe the earlier formative stages of the acute suppurative pleurisy as an empyema is just as wrong as to describe the early stages of an acute septic cellulitis as an abscess before a localized collection of pus has formed. No one would question the fundamental importance of paying attention to the stages of development of an acute septic cellulitis in discussing treatment. It is no less fundamental to consider the stage of development of the suppurative pleurisy in discussing the treatment of "empyema." In discussing the treatment of a mature empyema, we must also discuss the treatment of the earlier acutely infected pleura. The term empyema should cease to be used as synonymous with the whole process of septic pleural infection and should be reserved for the mature condition or residual abscess which results.

This failure to understand the pathology of pleural infection is responsible for much of the confused thought and advice that has reappeared with the introduction of chemotherapy, and notably of penicillin. The effect, and indeed the success or the first division within the cyst, the reduction takes place and when, after a second division, the four new flagellates emerge, they are haploid organisms. But there is nothing left over and no death of the organism.

There is a large group of Protozoa—the ciliates, which are relatively speaking highly organized. They have all the essentials: a sensitive and elaborate system of co-ordinated movement—an excretory system and a simple but adequate digestive mechanism composed of acid-secreting vacuoles. The ciliates conjugate by the exchange of nuclei and then each proceeds upon its way after some rather complicated internal nuclear rearrangements. The complete individual is in each case preserved.

Some excellent workers in America, belonging to the school of Calkins, Woodruff and Jennings, in their determination to find the end of the span of life in these organisms, spent literally years of their lives observing the rate of division under conditions in which conjugation did not take place, in the hope that the strain as a whole might show old age and die. The ciliates however, so long as the food supply was adequate, wore out the observers and would not themselves show senescence.

It must be admitted that the ciliates have, in addition to conjugation, an individual nuclear reorganization, a sort of spring cleaning called endomixis but this does not do away with the fact that only starvation or violence puts an end to the ciliate itself.

Now, can it be claimed that although the corpse cannot be produced, the span of life is the number of hours intervening between two divisions? That is to say that, when A has produced A_1 and A_2—A is dead. I think that is fantastic as the *whole* actual substance of A is still growing and functioning alive in A_1 and A_2.

So the choice must be made, either the Paramœcia in my watch glass, for example, are never more than twenty-four hours old, or the individual I am now looking at has itself existed for millions of years since it first gradually developed out of the original slime.

It would seem, therefore, that as long as there is no differentiation which sets apart the reproductive from the non-reproductive cells, there is no end to the span of life except through starvation or violence. The surviving organisms are the original creatures.

It must be admitted that even the rather highly organized ciliates have what some people would consider a low standard of living. Therefore it would appear that if you want but little here below, you can get that little, long.

Dr. R. E. Rewell: In this discussion attention has been directed entirely to those individuals of any species which survive the longest, even those living to what may be called the "average span" have been neglected. We have been reminded of the high mortality among human infants and its well-known decrease with improving external conditions with a resulting rise in the average expectation of life at an early age. It has been held usually that very long-lived individuals are no less common in savage than in civilized communities, though he appears to have shown that this may not be the case.

A distinction has been drawn between those causes of death which may be ascribed to accident and those to more fundamental causes. However, in many cases this distinction is not clear. Thus in the case of a human infant dying of bronchopneumonia it may be that the infant is unduly susceptible, that particularly virulent micro-organisms are present in its environment or it may have been chilled. With young organisms, moreover, it is impossible to deduce longevity in the stock from the length of survival of the offspring.

It is noteworthy that in different species degenerative changes in different organs limit the length of life. Thus in man vascular catastrophes from degenerative changes in the arteries are a frequent cause of death in middle life, but in other mammals such changes are far more rare, though I have seen lesions resembling Mönckeberg's sclerosis in a Mitchell's Wombat aged over 20 years. (Sections of liver and kidney of an aged Pine Marten were demonstrated to show the absence of degenerative changes in the arterioles.)

(iii) An illness complicating measles or whooping-cough.

(iv) A streptococcal or staphylococcal infection.

(v) The duration of the pleuro-pulmonary process; it is rare for maturation to occur in less than two to three weeks.

(vi) The gravity of the illness; a patient who is profoundly ill or has recently been profoundly ill needs very careful assessment.

(vii) When the temperature chart is of the remittent or sustained type indicating an invasive infection rather than the swinging septic type of mature suppuration.

(viii) The character of the aspirated fluid. The proportions of sediment and supernatant fluid are often a good guide to the stage of the pleural illness.

Finally it must be stressed that drainage of an empyema is never an emergency unless there is a bronchial fistula big enough to produce a risk of flooding the lungs. It is, of course, always desirable to drain pus as soon as its presence is recognized, but it is not a true emergency. If there is any doubt as to maturation of the process it is always safer to delay for a few days and to relieve symptoms by aspiration or by intercostal drainage. Thorough and repeated aspiration is an essential part of the management of the formative phase for even if it does not achieve cure of the pleural suppuration it should at any rate result in a smaller residual empyema that will heal correspondingly more quickly.

(*B*) *The provision of adequate drainage:* Once more it must be stressed that much of the difference of opinion about the success of simple aspiration or of intercostal drainage as opposed to rib-resection arises from failure to appreciate the importance of the stage of the illness in which each method is used. Many of the cures of "empyema" by aspiration are really cures of early pleural infection. It is much less likely that a mature or nearly mature empyema can be cured by aspiration alone, simply because of the adverse mechanical factors present in the thick exudate, rigid or partly rigid walls and massive fibrin clots. Conversely, drainage by rib-resection in the early stages is not only unwise but dangerous. It is the failure of recognition of this that still leads to statements that rib-resection is very dangerous in infants and should not be done. The margin for error in them is small and a too early rib-resection will often kill. On the other hand my experience is that a mature empyema in an infant demands drainage by rib-resection just as much as in an adult.

Aspiration and intercostal drainage, so valuable as temporary measures, can never function satisfactorily when fibrin masses are present, and to persist in their use not only prolongs the patient's illness unnecessarily but also exposes him to the grave risk of a chronic empyema. We are always seeing new suggestions or reading descriptions of complicated apparatus, the object of which is to suck pus out through a small hole rather than let it come out freely through a larger hole. The advocates of these hole-in-the-corner methods should remember that rib-resection is needed for proper pleural toilet as well as for the insertion of an adequate drainage tube. The exposure that rib-resection alone can give is essential for certain and rapid healing in almost all cases of mature empyema.

Not only must the drainage hole be big enough but it must be in the right place if drainage is to be sufficient and the siting of the hole must always be carefully considered. It is a sound plan to introduce lipiodol and air at the time of aspiration of pus and then to take radiographs in postero-anterior and lateral planes in order to delineate the upper and lower extent and the shape of the cavity. In a typical posterior basal empyema drainage should be (*a*) in the paravertebral gutter just lateral to the angle of the rib, (*b*) not lower than the 9th rib as otherwise the drainage track may be shut off as the diaphragm rises during healing.

failure, of penicillin will be greatly influenced by the stage of evolution of the pleural suppuration. Its exhibition in the early "cellulitic" phase is more likely to be followed by successful control of the process than in the later stages when there is an abscess with thick pus, walls covered with tough exudate and often fibrin clots or purulent masses lying in the cavity. This should be self-evident and yet from many published accounts it is clear that the authors have not realized it.

The great benefits of penicillin therapy are so obvious that they need no emphasis, though it must not be forgotten that penicillin does one thing and one thing only—it kills certain bacteria provided always it can get to them. It can control or sterilize a bacterial battlefield in the body. On the other hand it is not a scavenger, it cannot clear up the battlefield. The body resources must serve this function, but there are times when the correction of the secondary mechanical effects of infection is too much for the bodily resources. That is why surgeons are still needed; that is why penicillin, although a great friend and a strong weapon, will never replace the surgeon. When mechanical derangements remain his help is needed. To delay or to withhold surgical help to clear up the battlefield is to harm the patient; at the least increasing the morbidity of his illness and often causing his death.

(2) *The fundamentals of treatment of pleural infection.*—(*A*) Assessment of the correct time for drainage; (*B*) provision of adequate drainage; (*C*) institution of proper physical treatment; (*D*) decision as to the correct time to stop drainage.

(*A*) *The correct time for drainage:* A great deal follows logically from what has already been said about pathology. In the early formative stages of pleural suppuration drainage is both unnecessary and dangerous: unnecessary because with proper management by aspiration and chemotherapy (i.e. penicillin) it may be possible to achieve resolution without abscess formation. It is in this phase that the methods of penicillin therapy described by Fatti and Florey (1946) are most likely to be successful. It may be dangerous because, as was so ably pointed out by Graham as a result of study of the high mortality of pleural suppuration in the influenza epidemic of 1917 and 1918, the patient is often suffering not only from pleural infection but from one or several other serious infective processes as well. He may be almost overwhelmed by a severe invasive infection with pneumonia, septicæmia, pericarditis, &c. If this pleural effusion, by virtue of its gross mechanical presence, is allowed to dominate the clinical and therapeutic picture and it is drained too early, then the patient may be unable to withstand the extra mechanical strain thrown upon him and he may die. It is true that the dangers of draining a diffuse suppurative pleurisy in which no limiting adhesions have formed may be minimized or even avoided by some form of closed intercostal drainage. The method still remains a dangerous one, for in these very patients in whom the danger is greatest and the margin of safety is very small, the powers of tissue reaction are so low and enfeebled that the tissues seem to melt away around the tube and in a short time an open sucking wound is caused. Even if the patient survives premature drainage he is often left with a total empyema which, if not treated skilfully, will lead to long or even permanent invalidism and great physical deformity.

Space does not allow full discussion of the criteria of assessment of the correct time for drainage, but it must suffice to say that it is essential to consider carefully the stage of evolution of the pleural process. Features which must be especially considered are:

(i) The age of the patient; children under 5 and more particularly infants and toddlers with a pleural infection are often suffering from a severe invasive infection and great caution must be exercised.

(ii) The occurrence in an epidemic of influenzal type.

of the lung, and if the expansion of the lung is maintained by continuous pleural suction, these patients get well and can be completely healed in two to three weeks and are left with a virtually normal chest. The operation is a severe one but is well tolerated if performed with simultaneous blood transfusion.

It is necessary to consider whether this method could, with advantage, be applied to acute empyema in civil life. I think we have much to learn about this but at present I would say that if a case of pleural suppuration is conducted correctly in the formative stage and a relatively small residual empyema results, it is best treated on the orthodox lines described above. Open thoracotomy and decortication would seem to be unnecessarily severe and to introduce too big a risk, especially as many empyema patients have only just recovered from a severe and often debilitating illness. On the other hand cases occur in which a large, possibly multilocular, and perhaps neglected empyema is present. Simple drainage by rib-resection may mean many weeks or even months of drainage and great care must be expended in the manipulations of the tube, &c. I am sure that open thoracotomy and decortication in these patients offers much. It can give healing almost by primary intention, or at the worst will leave a small simple pocket to be drained.

I have been unable to do more than refer briefly to the big question of chronic empyema. It has been truly said that the best treatment of chronic empyema is not to let it occur. We should remember that if an uncomplicated acute empyema is treated carefully upon the simple and fundamental lines laid down above healing should be steady and progressive to complete cure. This complete cure can only be attained when the lung has been completely expanded to fill the whole of the cavity, and the visceral and parietal pleuræ are firmly fused together. At any moment in the course of healing it is possible for some quite simple fault to slow up or stop this natural and steady process. The fault may occur only too easily; it may be, for instance, that the drainage tube is incorrectly placed or incorrectly or unwisely adjusted or not adjusted at all. As a result the patient is placed in danger of developing or actually develops a chronic empyema. Simple and constant care and attention will prevent this, and if we appreciate that this is so we shall spare ourselves a great deal of anxiety and our patients much unnecessary suffering.

REFERENCE

FATTI, L., FLOREY, M. E., *et al.* (1946) *Lancet* (i), 257 and 295.

Mr. T. Holmes Sellors: The term "empyema" should only be used with the clear distinction of the actual pathology of the pleural condition.

It is realized that chemotherapy, in particular penicillin, can achieve good results in diffuse and early infection, but that its use in a local pleural abscess is open to definite limitations. Penicillin can certainly sterilize many of these abscesses, but it cannot obliterate the actual cavity, and persistence with it beyond a certain stage increases the liability to formation of a chronic thick-walled dead space.

To continue the story of treatment of the localized empyema after drainage, it is necessary to consider a method of closure of this cavity. In ordinary circumstances abscesses with soft walls, once they have been drained, close in steadily, but in the case of an empyema the outer wall is rigid, and in any case should not be allowed to collapse inwards. The underlying lung must be encouraged to expand outwards and make contact with the chest wall—but in such a way that the closure is complete and occurs without pocketing. When the fibrin-coated parietal and visceral pleural layers are in apposition, the empyema space may be regarded as healed, not before.

The deposit of fibrin on the cavity walls plays also a great role in the healing process. If there is any delay in correct handling, this fibrin organizes into firm

(C) *Physical treatment:* An empyema is but an abscess in a special site and like an abscess anywhere else in the body depends for its healing, once adequate drainage has been provided, on approximation of its walls. One object of *adequate* drainage is, of course, to allow this approximation to proceed unchecked. Delay in instituting adequate drainage by persisting in aspiration too long, results in greater thickening of the walls and the process of approximation is either greatly prolonged or completely prevented. In an abscess elsewhere the walls usually fall together concentrically but this must be avoided at all costs in empyema. The obliteration of the empyema should be achieved by *expansion* of the lung and not by falling in of the chest wall and displacement of the mediastinum and diaphragm. Indeed the rapidity of expansion of the lung is directly influenced by preventing the chest wall and diaphragm from becoming rigid and contracted and by promoting their movement and thus their expansile action. To this end, therefore, early and meticulous physical treatment is fundamental.

Physical treatment consists of four parts:

(*a*) General exercises to improve general muscular and bodily tone.

(*b*) Arm and shoulder movements to prevent stiffness.

(*c*) Postural supervision to prevent scoliosis.

(*d*) Breathing exercises to prevent fixation of the ribs and diaphragm and to ensure early and rapid expansion of the lung. A patient, far from suffering diminution of respiratory function after an empyema, should actually improve it if proper physical exercises are given.

The modern breathing exercises are simple, and are directed towards maximum concentration on the affected zone without great and unnecessary expenditure of energy as in the older exercises. Properly taught and graded they are no strain even to a very ill patient immediately after operation. All the attendants must see that the patient practises them regularly throughout the day and not just when the masseuse comes. Five minutes every hour should be the slogan.

It follows, also, that the treatment of an empyema should be ambulatory. Many patients are kept in bed as long as the drainage tube is retained. This is quite wrong; unless there is some contra-indication on medical grounds the patient should be got up within a few days of operation.

(D) *When to stop drainage:* Fortunately it is now far less common to see the drainage tube removed in an empiric or arbitrary time, such as two weeks. There is only one safe time to remove the drainage tube and that is *when a cavity can no longer be demonstrated to exist in the pleura.* If the tube is removed before this, then there is great risk of a chronic empyema following. Too early removal of the tube is indeed the commonest cause of chronicity of an empyema. There are many important practical details in connexion with the management of the tube. The interest of the surgeon inexperienced in empyema will be greatest immediately after operation and become less and less as the days or weeks pass by; very often after a few weeks his interest is nil and he leaves the management of the important phase of removal of the drainage tube to someone else. The surgeon experienced in empyema knows that his personal interest in the case must *increase* as the days pass by.

Decortication in the treatment of acute empyema.—Perhaps the most important thing we have learnt in chest surgery from the war is the great success that can follow early evacuation of clot and decortication of the lung in an infected hæmothorax. A patient gravely ill with a chest full of breaking-down infected clot, often with a heavy mixed and foul anaerobic infection, if treated by aspiration or by drainage alone either dies or drifts into chronicity. If treated by open thoracotomy and decortication

The old teaching of removing a tube each day for boiling, and then replacing it was one of the most productive causes of chronic empyema. Sooner or later the original tube could not be replaced, and a smaller one was inserted, and so on, until a pin-point sinus was left to drain large spaces.

If the sinus becomes unduly small a laminaria or sea-tangle tent can be used, and the swelling of this may in twenty-four hours enlarge a narrow opening to an appreciable extent.

It has already been mentioned that, if the tube is kept too short, the thickening parietal pleura may grow over the internal opening. Similarly, too long a tube may impinge on the lung and lead to ulceration. The maintaining of a tube of adequate bore is, of course, essential, and the standard method of using a safety-pin and narrow length of strapping for holding the tube in position on the chest wall should be adopted as a routine. A simple corset dressing over one or two thicknesses of gauze is all that should be needed to cover the tube. Elaborate dressings or many-tailed bandages should never be employed.

The decision as to the time of tube removal is actually simple. No empyema cavity must remain, and the only opening should be a narrow track through the chest wall. It is possible when closure is obviously nearly complete to replace the wide tube by one of smaller bore just before the final removal.

The *bacteriology* of the discharges should be examined at intervals. It is realized that extensive drainage leads to secondary infection in spite of all precautions that may be taken with dressings, and the most common organisms encountered in this respect are *Ps. pyocyaneus* and *B. proteus*. On culture these act as "spreaders" and may mask a more harmful pathogenic organism. If selective cultures can be obtained, an organism responsive to chemotherapy may be encountered. We have not found that antiseptic or antibiotic substances in paste or cream form have had any direct local benefit, though their systemic use has been valuable.

Irrigation was at one time in considerable favour, but when a careful pleural toilet has been made its value is limited, and it is moreover dangerous in the presence of a bronchopleural fistula, when the irrigating fluid might easily enter the lung.

The presence of a bronchopleural fistula is easily recognized on a pleurogram, and is a common occurrence during the course of empyema treatment. It is, however, of little importance unless of considerable size, or dependent for its origin on some additional pathological factor such as new growth or tuberculosis. These fistulæ may delay healing to a small extent, but ultimately heal spontaneously under the ordinary process of drainage and gradual closure of the empyema cavity.

Chronic empyema is too large a subject to be discussed in any detail, though its most common cause, namely poor handling of the acute phase, has been mentioned.

The treatment is basically the same: active inspiratory exercises for lung re-expansion plus adequate and controlled drainage.

I have not done a thoracoplasty or extensive operation on any chronic empyema for the past eight years, though some patients have taken a year or eighteen months to heal. A limited small operation in the form of local muscle graft may hasten the final closure, but in the non-tuberculous cases I have not found major surgery necessary, so long as enough time is given to adequate conservative treatment.

During the period of healing the general condition of the patient should not be ignored. A secondary anæmia is a very common finding and may require blood transfusion. The estimate of blood proteins may also show a low figure, which should be countered by a high protein intake, possibly with some of the more palatable cicatrizing tissue, which is laid down in greater thickness on the chest wall side than on the lung, but in both cases it is a powerful deterrent to obliteration of the cavity, and is an important factor in the formation of the chronic empyema dead space.

Parietal fibrosis results in pulling down of the ribs and their approximation with resultant scoliosis. The actual shape also alters, becoming triangular instead of flat, and it can be understood that full functional restoration is only possible if there have been no structural or skeletal changes.

The prevention of the chronic empyema lies therefore in two main factors: (1) The maintenance of adequate drainage until the cavity is obliterated, and (2) breathing exercises and physical treatment to encourage the lung to re-expand and restore respiratory function.

Breathing exercises are absolutely essential. They are based on active, powerful and concentrated inspiratory efforts. The movement of the chest wall itself is a very good index to lung function, and if the chest wall can be made to move freely it can be assumed that underlying lung expansion is good. These inspiratory exercises require a voluntary control of an area of the chest wall. This is operated by working against pressure of the physiotherapist's hand, and later the pressure is given by the patient himself. The exercises can be started from the very onset of the condition and carried out with increasing vigour day by day. They must be done regularly for five or ten minutes every hour, and with the utmost concentration.

At the same time there is no need to maintain patients in bed once their general condition permits movement. More general physical exercises become possible, and can be worked up in classes. The use of webbing belts to help the breathing exercises has been found valuable, and, as an adjunct, regular measurement of the vital capacity and a general competitive spirit are a considerable stimulus. The patient by the time of closure of the cavity should not only have as good a respiratory function as the normal individual—it should be better.

The other factor is the handling of the tube and *closure of the cavity*. Obliteration may take place uniformly and speedily, but uneven expansion may lead to "bottle necks" and a number of unusual shapes. The correctly placed tube lies so that discavity drainage is always possible, and after the first day or two the amount of discharge from that tube should be minimal. Free drainage suggests that a dependent or unrecognized pocket will have to be dealt with. It is not possible to visualize actually what is happening through the chest wall, so we have to depend upon other methods to gauge the healing process of the empyema. A gloved finger or soft bougie is sometimes useful, but we have come to depend on radiography and the use of contrast media—in other words, the pleurogram. Two-plane radiographs are taken after the cavity has been filled with a radio-opaque oil (incidentally barium emulsion is permissible if there is no bronchial fistula). Pleurograms should be made when the outline of the cavity cannot be visualized on the ordinary radiograph, and should then be repeated at regular intervals, say ten or fourteen days, until complete closure is obtained, and after each pleurogram has been made the tube adjustment can be safely considered. A "bottle neck" easily forms if the tube is not through the full thickness of the chest wall, or if the basal expansion occurs more readily than that of the apex. In such a case the tube would have to be lengthened, so that its open end lies within a short distance of that of the apex of the pocket. In other cases a dependent arm or limb may require secondary drainage to ensure its healing, and a rapid axillary expansion may leave a "horse-shoe" or "circular" form of track whose closure has to be carefully watched.

The actual *handling of the tube* must be regarded as an important technical exercise. Any alteration in the position, length or size of the tube must be most carefully studied.

The old teaching of removing a tube each day for boiling, and then replacing it was one of the most productive causes of chronic empyema. Sooner or later the original tube could not be replaced, and a smaller one was inserted, and so on, until a pin-point sinus was left to drain large spaces.

If the sinus becomes unduly small a laminaria or sea-tangle tent can be used, and the swelling of this may in twenty-four hours enlarge a narrow opening to an appreciable extent.

It has already been mentioned that, if the tube is kept too short, the thickening parietal pleura may grow over the internal opening. Similarly, too long a tube may impinge on the lung and lead to ulceration. The maintaining of a tube of adequate bore is, of course, essential, and the standard method of using a safety-pin and narrow length of strapping for holding the tube in position on the chest wall should be adopted as a routine. A simple corset dressing over one or two thicknesses of gauze is all that should be needed to cover the tube. Elaborate dressings or many-tailed bandages should never be employed.

The decision as to the time of tube removal is actually simple. No empyema cavity must remain, and the only opening should be a narrow track through the chest wall. It is possible when closure is obviously nearly complete to replace the wide tube by one of smaller bore just before the final removal.

The *bacteriology* of the discharges should be examined at intervals. It is realized that extensive drainage leads to secondary infection in spite of all precautions that may be taken with dressings, and the most common organisms encountered in this respect are *Ps. pyocyaneus* and *B. proteus*. On culture these act as "spreaders" and may mask a more harmful pathogenic organism. If selective cultures can be obtained, an organism responsive to chemotherapy may be encountered. We have not found that antiseptic or antibiotic substances in paste or cream form have had any direct local benefit, though their systemic use has been valuable.

Irrigation was at one time in considerable favour, but when a careful pleural toilet has been made its value is limited, and it is moreover dangerous in the presence of a bronchopleural fistula, when the irrigating fluid might easily enter the lung.

The presence of a bronchopleural fistula is easily recognized on a pleurogram, and is a common occurrence during the course of empyema treatment. It is, however, of little importance unless of considerable size, or dependent for its origin on some additional pathological factor such as new growth or tuberculosis. These fistulæ may delay healing to a small extent, but ultimately heal spontaneously under the ordinary process of drainage and gradual closure of the empyema cavity.

Chronic empyema is too large a subject to be discussed in any detail, though its most common cause, namely poor handling of the acute phase, has been mentioned.

The treatment is basically the same: active inspiratory exercises for lung re-expansion plus adequate and controlled drainage.

I have not done a thoracoplasty or extensive operation on any chronic empyema for the past eight years, though some patients have taken a year or eighteen months to heal. A limited small operation in the form of local muscle graft may hasten the final closure, but in the non-tuberculous cases I have not found major surgery necessary, so long as enough time is given to adequate conservative treatment.

During the period of healing the general condition of the patient should not be ignored. A secondary anæmia is a very common finding and may require blood transfusion. The estimate of blood proteins may also show a low figure, which should be countered by a high protein intake, possibly with some of the more palatable casein hydrolysates, and at regular intervals a complete assessment of the patient's general condition as well as the local lesion should be made.

A tragic complication is the occurrence in a small proportion of cases of cerebral abscess. This does not occur in the acute stages, but in the more chronic ones. If there is any secondary hæmorrhage, the patient should be put at complete rest, and if there are any complaints of headache or dizziness these should be investigated immediately.

In conclusion, it should be realized that chronic empyema is a severe and distressing disability which in the majority of cases is occasioned by mishandling of the acute phase.

[*March 5, 1947*]

The Packing of Abdominal Incisions in Peritonitis

By IVOR LEWIS, M.S.

ONE night five years ago I was operating on a bad perforated appendix and was just closing the peritoneum when the patient collapsed. Fearing a death on the table I packed the wound with gauze, stuck some strapping over it and got the patient back to bed. To my surprise he recovered and was discharged four weeks later with his wound neatly healed. This incident prompted me to try the method again in cases of foul peritonitis. I had, from time to time, seen claims made for packing the abdominal wall in peritonitis—but had dismissed them as cranky and dangerous. In 1929 Garlock advocated leaving the wound wide open, occasionally putting a few sutures in the peritoneum, and in 264 cases reported only 6% incisional hernias compared with 15% by Bartlett, who sutured such wounds in the same hospital. Gamble and later Coller have also commended the practice. Gradually I came to use the method quite often as the cases healed well and smoothly.

Description of procedure.—Where there is offensive or thick pus the abdomen is drained and the abdominal incision packed. My incision of choice for appendicitis is McBurney's. For drainage a suprapubic stab wound is made and a ribbed rubber drain used. The peritoneum, together with available extraperitoneal tissue and transversalis fibres, is firmly sutured with a continuous catgut, in such a way that the suture line is watertight. Vaseline gauze is then laid in the wound lightly and three strips of strapping placed firmly across it. A separate dressing is placed over the drain, and the operation is over. Silk or cotton is to be avoided, but I have used *fine* nylon in many of the cases—with trouble from a sinus only once. Lately I have also used silkworm gut—the ends threaded over buttons on each side of the wound. The suture can then be removed at the end of a fortnight. The wound is not touched for five days. It is then re-dressed on alternate days. At the end of a week it is a deep gutter lined by clean granulation tissue, exuding a little pus. At the end of a fortnight it is a narrow chink, and in three weeks it is a linear wound flush with the skin and largely healed over.

After-treatment.—Normal "clean stitch" appendicitis cases I like to get up on the first day. These septic cases, however, have been kept in bed for three weeks, mainly because they are ill, not because of the abdominal wound. (Mere getting up does not, of course, put any particular strain on the abdominal incision.) Recently I have allowed some patients up at the end of a fortnight. The wound is throughout kept firmly strapped and the abdomen firmly bandaged. The drain is left in for three days, or longer if the pus is thick.

The patient is usually fit for discharge with a simple dry dressing during the fourth week.

Indications.—In the nature of things most of the cases will be appendix peritonitis, where the pus is foul or thick. Particularly dangerous is suturing the muscles where the appendix is a bluish-black slough suggesting heavy anaerobic infection. Incidentally a number of cases of fatal gas-gangrene of the abdominal wall have been reported in such patients. Offensive peritonitis from any other origin may with advantage be treated thus, provided the incision is suitable. I have treated gangrenous strangulated hernias with contamination, perforated stercoral ulcer, and a late perforated duodenal ulcer.

The incision.—The disruptive strain on a vertical incision is several times as great as that on a transverse. Moreover the sutures, as they take the fibres of the aponeurosis lengthwise rather than across, cut out more easily. I have, therefore, used the method only a few times in vertical incisions, although the results have been satisfactory, except for one disruption. I consider that packing a vertical wound is not a reasonable proposition where much post-operative distension is likely. The gridiron incision is ideal for natural strength. Any transverse incision is, however, suitable and oblique incisions for hernia can also be treated thus with safety, though the hernia may be expected to recur later, as it will anyhow with sepsis.

Results.—We have used the method at the North Middlesex Hospital in 64 cases in the last five years. Of the appendix cases, three died post-operatively: two of peritonitis on the second day and one of peritonitis, obstruction, and burst belly on the tenth day. This last patient should not have been selected as she had a vertical mid-line incision and was distended from peritonitic obstruction.

We have used it five times in gangrenous strangulated hernia with contamination. One died and a hernia recurred in two patients. Three hernias have occurred in the appendix cases, 20 of which have been done less than a year. The rarity of scar hernias has, so far, been the most surprising fact. The cases have run a very smooth course, the pain, distension and temperature steadily subside within a few days; so striking has this been that it makes one wonder how far the critical post-operative worsening so often seen in peritonitis cases is due to abdominal wall cellulitis and inadequate drainage. The packed wound is painless and free from œdema. There is no undermining or pocketing. The scars are strong and linear—far superior in strength and appearance to those *sutured* under septic conditions.

Comments.—(*a*) The method differs from that used by Garlock in making a special point of firm suture of the peritoneum plus any convenient fibres of transversalis fascia. A watertight continuous suture prevents further pus oozing into the wound from the peritoneum.

(*b*) To suture an infected abdominal incision seems to be bad procedure because: It dams up the pus causing it to spread along the intermuscular and extraperitoneal planes. It strangles the swollen tissues, causing sloughing of fascial strands. Often an intramural abscess forms which may burst externally or even inwards into the peritoneum laying the foundation for a hernia. The appearance of the wound is only too well known—œdematous, angry, painful, with pus oozing from every pore. Surgeons are no longer in any doubt of the desirability of leaving open heavily contaminated wounds in other parts of the body. In the abdominal wall they have felt that the strain on the healing wound overrides all other principles of good surgery. In my experience such wounds can, with advantage, be left open provided they are properly directed.

(*c*) On what does the strength of an abdominal scar depend? The answer is "on the integrity of the serotransversalis". Studies of disruption of abdominal wounds and of the evolution of scar hernia show this conclusively. Scar hernias are not due to stretching of a scar; they are due to a concealed disruption of the wound in the early post-operative period. The surgeons who have the post-operative hernias are those who have the burst abdomens.

(*d*) It is widely believed that healing by second intention is necessarily inferior, weaker or untidier, than healing *per primam.* But the choice in a case of peritonitis is really between healing by granulation under good conditions (open treatment) and under bad conditions (closure and with devitalized tissues).

The Concentration of Penicillin in Bile

By E. G. TUCKWELL, F.R.C.S.

PENICILLIN is antibiotic to typhoid bacilli in high concentration varying with the strain of the organism. As attempts to cure typhoid carriers by administration of the drug have not been successful in spite of adequate concentration being demonstrated in the duodenal bile, my medical colleagues asked me to get samples of common duct bile after administration of a single large dose of penicillin.

That penicillin is concentrated in the bile duct much above serum levels was demonstrated by Florey (Abraham *et al.*, 1941) and his co-workers, using cats and rabbits after subcutaneous or intraduodenal administration.

Rammenkamp and Helm (1943) collected human bile by means of a duodenal tube to show that after intravenous injection of 20,000 units of penicillin the bile contained concentrations higher than serum. To one patient who had a cannula in the common bile duct they gave 20,000 units of penicillin intravenously and found 1·25 units/c.c. in the bile fifteen minutes later, the level falling to zero in 150 minutes.

Struble and Bellows (1944) found a concentration of 6·65 units/c.c. in the bile collected by a duodenal tube after "a single massive intravenous dose of penicillin". The bile retained its concentration for three hours. In order to get bile concentrations up to the antityphoid level we decided to give a single intramuscular injection of 250,000 units in 1 c.c. of water. Four patients, who had undergone cholecystectomy and choledocholithotomy with insertion of a T-tube into the common duct, were given this dose and the bile collected continuously as it drained down the tube. At the end of each period of one hour the test-tube containing bile was replaced by a new one. The experiment was continued for six to eight hours. Assay of the penicillin in bile was carried out by Dr. R. Shooter, to whom I am very grateful for helpful advice, using the cylinder plate method and comparison with known strengths of Oxford staphylococci.

The results of three such excretion experiments are shown on the graph (fig. 1). It will be noticed that they vary in height, but that the rapid rise is to a peak period with a rapid fall again. The concentration in all three cases is above serum levels, but not maintained—their peak period is between the second and third hour in two cases, and this seems to be the general impression formed by other observers. In one patient the peak occurred after seven hours; he had had severe and repeated attacks of jaundice for many months and the excretion was observed five days after removal of common duct stones.

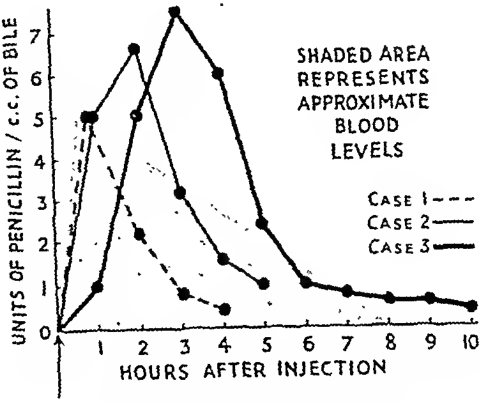


FIG. 1.—250,000 units of penicillin injected intramuscularly. Specimens of bile collected continuously over each period of one hour.

On the chart, Case 1 (- - -) had fever and jaundice for ten weeks with operation two days before; Case 2 (—) had ten weeks' fever and jaundice and operation six days before; Case 3 (—) had only been jaundiced very recently and the estimation made five days after operation.

Concentration of penicillin is greatly reduced by any liver damage and Zaslow and others (1947) have shown that if the concentration in the common bile duct is low, or if no penicillin can be demonstrated, then liver function tests show liver damage not suspected by clinical examination.

Zaslow gave 15,000 units of penicillin intravenously to patients immediately before operation or cholecystectomy. The gall-bladders were removed entire and the contained bile assayed for penicillin. His results show that the penicillin concentration in the gall-bladder was equal to, or lower than, that in the common duct, but that if the cystic duct was obstructed by stone or inflammation then the penicillin did not appear in the gall-bladder at all and was unlikely to be effective in the treatment of empyema. These gall-bladders were all pathological and my very small experience has led me to believe that a normal healthy gall-bladder will concentrate the penicillin to a greater level than that in the common duct.

I selected two patients, with apparently normal liver function, who were to undergo partial gastrectomy for peptic ulceration. 250,000 units of penicillin in 1 c.c. water were given intramuscularly two and a half hours before the estimated time of operation. Immediately the abdomen was opened samples of bile were aspirated from the gall-bladder and in one case from the common duct also; in the other case the local adhesions from a duodenal ulcer made the common duct difficult of access and I abandoned the attempt. In the first patient gall-bladder bile showed a concentration of 25 units penicillin/c.c. bile at the same time that common duct bile showed 10 units penicillin/c.c. bile—two and a half hours after the intramuscular injection. In the second patient gall-bladder bile showed a concentration of 8 units penicillin/c.c. bile two and three-quarter hours after injection.

These figures suggest that a healthy gall-bladder can concentrate penicillin to a strength which may be lethal to the typhoid bacillus, but that any liver impairment, or damage to the gall-bladder, will make these concentrations unlikely. In any event the administration must be repeated frequently to maintain a high concentration in the bile (a continuous drip of 1,000,000/three hours).

Streptomycin apparently behaves just like penicillin; we have only given it to one patient with common duct drainage but she had a good concentration at three hours and some still present at six hours. Zaslow got the same results from streptomycin as he got from penicillin, namely, that none appeared in the gall-bladder if the cystic duct was obstructed, and that levels in pathological gall-bladders were equal to, or slightly lower than, those in the common duct.

De Bakey and Pulaski (1946) have attempted to treat two typhoid carriers with streptomycin without success.

In conclusion I may say that high concentrations of penicillin in the common bile duct, above 6 units/c.c., depend on large dosage and good liver function, this high concentration is very transient and probably appears between the second and third hours. High concentration of penicillin in the gall-bladder depends both on liver function and the patency of the cystic duct; if these factors are satisfactory very high concentration may be obtained, but how long it is maintained I do not know.

REFERENCES

Abraham, E. P., Chain, E., Florey, H. W., *et al.* (1941) *Lancet* (ii), 177.
de Bakey, H. E., and Pulaski, E. J. (1946) *Surgery*, 20, 749.
Rammenkamp, C. H., and Helm, J. I. (1943) *Proc. Soc. exp. Biol. N.Y.*, 54, 31.
Struble, G. C., and Bellows, J. G. (1944) *J. Amer. med. Ass.*, 125, 685.
Zaslow, J., *et al.* (1947) *Surg. Gynec. Obstet.*, 84, 16 and 140.

Section of Pathology

President—A. B. Rosher, M.R.C.S., L.R.C.P., D.P.H.

[*March* 18, 1947]

DISCUSSION: THE LABORATORY DIAGNOSIS OF VIRUS INFECTIONS

Professor A. W. Downie, Liverpool: *Laboratory diagnosis of smallpox.*—Although smallpox in its typical form may be relatively easy to diagnose clinically, recent experience in this country has served to emphasize the difficulties which face the clinician when the disease occurs in vaccinated persons. In such instances the infection may run a mild and atypical course and it is in these cases that the laboratory can offer valuable aid. The methods available to the laboratory worker and the precautions to be taken in the collection of specimens have already been set out (Downie, 1946), and it is proposed here to discuss the merits and disadvantages of the various methods in the light of extended experience.

Examination of stained smears from skin lesions.—The value of this method in the early stage of smallpox infection has been stressed by van Rooyen and Illingworth (1944). The usefulness of the test depends on the careful preparation of smears and the instructions of van Rooyen and Illingworth should be followed. When pustulation has occurred the results are not so reliable, as elementary bodies in these smears appear to be much less numerous and their presence tends to be obscured by other particulate debris in the exudate. Smears should be allowed to dry and sent to the laboratory without fixation or other treatment, and as such smears from smallpox cases contain living virus (Downie and Dumbell, 1947*a*), care should be taken in packing and despatching the slides. At least two slides should be sent from each suspected case so that the material on one may be used for the inoculation of the chorio-allantois of developing chick embryos as described below. If the preparations have been properly made and stained by Paschen's or Gutstein's method, the finding of numerous typical elementary bodies may be valuable evidence in support of a diagnosis of variola. Some experience is necessary for the correct evaluation of the microscopic findings and it should be emphasized that one cannot, by microscopical examination alone, identify the elementary bodies of a particular virus; as always in such laboratory tests, the results of the examination of smears must be considered together with the clinical picture and the epidemiological data available. It should, however, be added that in smears made from the lesions of virus infections such as herpes simplex, herpes zoster and chicken-pox, elementary bodies are usually scanty and do not stain as readily as those of variola. The elementary bodies of vaccinia are indistinguishable from those of variola and consequently the examination of smears will not help to distinguish a case of atypical variola from secondary vaccinial lesions occurring in a recently vaccinated person. During the past two years I have examined smears from 24 cases of smallpox (*see* Table I) in addition to numerous

Table I.—The Results of Laboratory Tests on Specimens from 61 Cases of Smallpox.

	Microscopical examination of smears	Inoculation on chorio-allantois	Serological test for antigen	Test of serum for antibody
No. of patients	24	29	31	34
No. of specimens	25	37	41	39
Specimens positive	13	35	40	37

Material was not available for all these tests in each of the 61 cases, but, with one exception, one or more of the tests was positive in every case.

These figures suggest that a healthy gall-bladder can concentrate penicillin to a strength which may be lethal to the typhoid bacillus, but that any liver impairment, or damage to the gall-bladder, will make these concentrations unlikely. In any event the administration must be repeated frequently to maintain a high concentration in the bile (a continuous drip of 1,000,000/three hours).

Streptomycin apparently behaves just like penicillin; we have only given it to one patient with common duct drainage but she had a good concentration at three hours and some still present at six hours. Zaslow got the same results from streptomycin as he got from penicillin, namely, that none appeared in the gall-bladder if the cystic duct was obstructed, and that levels in pathological gall-bladders were equal to, or slightly lower than, those in the common duct.

De Bakey and Pulaski (1946) have attempted to treat two typhoid carriers with streptomycin without success.

In conclusion I may say that high concentrations of penicillin in the common bile duct, above 6 units/c.c., depend on large dosage and good liver function, this high concentration is very transient and probably appears between the second and third hours. High concentration of penicillin in the gall-bladder depends both on liver function and the patency of the cystic duct; if these factors are satisfactory very high concentration may be obtained, but how long it is maintained I do not know.

REFERENCES

Abraham, E. P., Chain, E., Florey, H. W., *et al.* (1941) *Lancet* (ii), 177.
de Bakey, H. E., and Pulaski, E. J. (1946) *Surgery*, 20, 749.
Rammenkamp, C. H., and Helm, J. I. (1943) *Proc. Soc. exp. Biol. N.Y.*, 54, 31.
Struble, G. C., and Bellows, J. G. (1944) *J. Amer. med. Ass.*, 125, 685.
Zaslow, J., *et al.* (1947) *Surg. Gynec. Obstet.*, 84, 16 and 140.

examination. Of specimens from infections other than smallpox only three produced typical virus infections of the chorio-allantois. One yielded the strain of herpes simplex referred to above and the other two produced characteristic vaccinial lesions. These latter two specimens came from secondary vaccinial vesicles in smallpox contacts who had been vaccinated some days previously.

Serological test for variola antigen.—The test which we have used as a routine is the complement-fixation test based on the technique recommended by Craigie and Wishart (1936). This test is more sensitive than the precipitation test and gives highly satisfactory results if suitable material is submitted for examination. As recommended by Craigie and Wishart the contents of at least six vesicles or pustules or the crusts from at least six lesions should be submitted to the laboratory. Extracts of these materials are tested against a hyperimmune antivaccinial serum prepared in the rabbit and this serum should have a satisfactory titre of antibody to the stable as well as to the labile component of the variola-vaccinia antigen. The test can be completed within twenty-four hours of receipt of the specimen but is obviously not of value during the papular stage of the disease; nor will the test serve to distinguish the antigen in vaccinial from that in variolar lesions. With these limitations the test is specific and reliable, although rather more material is necessary for examination than for the detection of virus by the chorio-allantoic inoculation test. The one negative result recorded in the table was due to the inadequate amount of material submitted and in this instance ''cultivation'' of the virus on the chorio-allantois was successful. Of many specimens submitted for test from patients suffering from diseases other than smallpox only one gave a positive reaction for variola-vaccinia antigen. This specimen came from a secondary vaccinial lesion and was one of the two mentioned above which produced typical vaccinial infection of the chorio-allantois.

Examination of the patient's serum for antibody to variola virus.—This test, like most examinations for antibody in the serum of patients convalescing from specific infections, is not so satisfactory as the previous tests which have as their object the identification of the infecting virus. Like all such tests it does not give a positive result in the early stage of the disease—within the first week after the onset of symptoms. Various tests for antibody are available but perhaps the most convenient utilizes the complement-fixation technique, the patient's serum being tested against either a vaccinial antigen prepared from skin lesions produced in rabbits or a variola antigen extracted from smallpox crusts. Of thirty-nine specimens of serum tested from 34 cases of smallpox, all except two gave a positive complement-fixation test for antibody (*see* table), the titres of the sera varying from 1 : 5 to 1 : 320. These samples were obtained from the eighth day of disease onwards. The two sera which gave a negative result were collected on the sixth and ninth days respectively after the onset of symptoms. Antibody may be detectable by this test in persons who have been vaccinated within the previous few months and, in tests on over 100 sera from such individuals, approximately 30% gave positive reactions with titres ranging from 1 : 5 to 1 : 80. The interpretation of a positive result will therefore be difficult in smallpox contacts who have recently been vaccinated. As antibody detectable by this technique seems to disappear from the blood within six months after vaccination, the test may be of diagnostic value after the first week of illness in persons who have not been vaccinated within the previous six months.

Summary.—Each of the laboratory tests described is of diagnostic value in individual cases depending on the stage of the disease. The examination of smears is particularly useful in the papular and vesicular stage if specimens are properly collected. The isolation of virus by the inoculation of material on the chorio-allantois of developing hens' eggs is an extremely delicate and reliable method but smears from various other conditions associated with skin lesions. In the majority of smears from smallpox cases elementary bodies were to be found and, when the smears had been properly collected from cases in the papular or vesicular stage, the microscopic appearances were characteristic; but in some which had obviously been made from the contents of pustules, the appearances were not as a rule sufficiently typical to be diagnostically helpful. In 9 of the 24 cases smears were made from vesicle fluid submitted for serological examination, and in three of these elementary bodies could not be found, although the fluid subsequently produced typical variola infection on the chorio-allantois of developing chick embryos. A negative result from the microscopic examination of such specimens can obviously be of no value in excluding a diagnosis of smallpox. The chief merits of this test are that it can be carried through within one hour, no elaborate apparatus is required and it is likely to be most helpful in the early stages of the disease.

Isolation and identification of the virus from smallpox cases.—The virus may be obtained from variola lesions by the inoculation of animals although the monkey is the only animal which is highly susceptible and the use of this animal is impracticable for routine diagnostic tests. Paul's test, which depends on the production of typical lesions on the cornea of rabbits after scarification and inoculation of infective material, has, in the hands of many workers, given rather irregular results. Within the last few years the chorio-allantois of developing chick embryos has been found to be highly susceptible to infection with variola virus from human sources (Irons *et al.*, 1941). Our own experience has convinced us that the technique of inoculation on the chorio-allantois is a very delicate test for the presence of variola virus (Downie and Dumbell, 1947*b*). When infective material from the scrapings of papules, from vesicle or pustule fluid or from crusts is inoculated on the chorio-allantois of ten- to thirteen-day chick embryos there appear, within two to three days' further incubation, characteristic lesions which differ in appearance from those produced either by vaccinia or by any other virus which multiplies in the chorio-allantois. The nature of the virus in the lesions can be confirmed by histological and serological tests. This method has as its chief disadvantages, (*a*) two or three days are required before a result is obtained, and (*b*) a supply of incubated fertile hens' eggs has to be available for a regular diagnostic service. The advantages of the technique are, (*a*) it is the most sensitive test at present available for the detection of variola virus, and (*b*) it offers the readiest means of distinguishing vaccinial from variolar infection. The viruses of chicken-pox and herpes zoster will not produce visible lesions on the chorio-allantois; the virus of herpes simplex, which we encountered once during these observations, produces smaller lesions on the chorio-allantois which histologically do not show in infected ectodermal cells the cytoplasmic inclusions which are present in the lesions due to the variola virus. Of 37 specimens from 29 cases of smallpox inoculated on the chorio-allantois, only two failed to produce typical variola lesions. One of these specimens gave a positive serological test for variola antigen and was examined before we had adopted the routine technique of mixing penicillin with the inoculum. The extract of the crusts in this case was found to be heavily infected with *Staphylococcus pyogenes* and consequently was treated with ether at room temperature for several days in order to destroy the bacteria before inoculation on the chorio-allantois. Subsequent tests showed that such treatment destroyed vaccinia virus and it seems likely that the failure to isolate virus was due to the ether treatment of the variola specimen. The other specimen which failed to infect the chorio-allantois was a single crust from a smallpox contact who had recently been vaccinated and in this case there was some doubt as to the diagnosis; insufficient material was available for serological test but a diagnosis of atypical variola was made on clinical grounds. Ten of the thirty-five specimens from which the virus was isolated on the chorio-allantois were insufficient for serological test and in five of these the material used for inoculation of eggs was obtained from dried smears sent for microscopic fluid, tracheal fluid and embryonic lungs. This method has opened up a new line of approach to the problem of influenza for this new medium, in which the virus will multiply, is not only economical and easy to handle, but devoid of latent viruses. Great progress has been made in the last few years in the development of this method until now it has become an extremely sensitive method of virus isolation.

The method adopted at the National Institute for Medical Research is that suggested by Beveridge and Burnet (1946). By the addition of antibacterial substances to the throat washing, filtration through a gradocol membrane is not necessary, the subsequent loss of virus is avoided and the maximum amount of virus allowed to come into contact with the respiratory epithelium. Throat washings containing 25% serum broth in saline are lightly centrifuged and are then inoculated direct into the amniotic cavity of 13-day chick embryos. Each egg receives 0·25 ml. throat washing and penicillin (100 units per ml.) and in addition 0·1 ml. of 5% sodium sulphamerazine. At least five eggs are inoculated with each washing as only a percentage become infected on primary, passage. After a further four days' incubation all surviving eggs are chilled in the ice-box and are then tested for the presence of virus. For this purpose, use is made of the phenomenon described by Hirst (1941) and independently by McClelland and Hare (1941) who showed that the influenza virus would cause agglutination of fowl red cells, thus providing a useful laboratory test for the presence of the virus. Burnet and Bull (1943) showed that the influenza A virus on primary isolation would agglutinate guinea-pig (or other mammalian) red cells to a higher titre than it would fowl cells; this they called the O-phase ("Original"). After passage, however, the ratio changed and fowl red cells were agglutinated to a higher titre; this was named the D-phase ("Derivative"). This change in ratio is referred to as the O-D variation. It is therefore necessary to test primary amniotic fluids with both species of red cells. This phenomenon of the O-D variation is not shown by the B virus.

This method is an extremely sensitive one for virus isolation and virus typing and is comparatively easy to carry out once the technical details have been mastered.

Indirect method: Titration of serum antibody.—(*a*) *Neutralizing antibody:* The result of infection with influenza is a rise in both neutralizing and complement-fixing antibodies in the serum. This can best be determined by measuring the rise in serum antibody between an acute and convalescent sample of serum. The determination of the antibody level of a single specimen of serum is of little value in the test for neutralizing antibodies as it does not take into account past clinical and subclinical infections. The most convenient method of measuring the neutralizing antibody in serum is that described by Hirst (1941). The test is based on the fact that the agglutination of fowl red cells by the influenza virus can be inhibited by serum and the agglutinin-inhibition level of the serum determined. The modification of Hirst's original method described by Salk (1944) has many practical advantages. A fourfold rise in antibody between an acute and convalescent sample of serum has until recently been regarded as indicative of infection, but in carrying out a large series of these tests during two epidemics, one is impressed by the large number of sera from typical cases of influenza which only show a twofold rise, or, in a few cases, no rise in antibody. There are several technical difficulties associated with these red cell agglutination tests but on the whole they do provide a valuable guide to the diagnosis of influenza and also reflect the incidence of infection in a community.

(*b*) *Complement fixation:* There is an increase also in the complement-fixing antibody as a result of infection. Hoyle and Fairbrother (1937) have described a method of carrying out this test using the soluble antigen of influenza prepared from mouse lung, which gives a result in many cases comparable to the neutralization method (Hoyle, 1945). The advances made in recent years in the study of influenza are essentially practical and the methods described can be carried out in most laboratories with advantage to our knowledge of epidemic influenza.

requires three days before a report can be made. The detection of virus antigen in vesicle fluid or crusts by the complement-fixation technique is a highly specific test for variola-vaccinia antigen and gives reliable results if sufficient material is submitted for examination. The test for antibody is likely to be useful after the first week of illness and only if the patient has not recently been vaccinated.

REFERENCES

CRAIGIE, J., and WISHART, F. O. (1936) *Canad. publ. Hlth. J.*, 27, 371.
DOWNIE, A. W. (1946) *Monthly Bull. Min. Hlth. and Emerg. Publ. Hlth. Lab. Serv.*, 5, 114.
——, and DUMBELL, K. R. (1947*a*) *Lancet* (i), 550; (1947*b*) *J. Path. Bact.*, 59, 189.
IRONS, J. V., BOHLS, S. W., COOK, E. B. M., and MURPHY, J. N. (1941) *Amer. J. Hyg.*, 33 B, 50.
ROOYEN, C. E. VAN, and ILLINGWORTH, R. S. (1944) *Brit. med. J.* (ii), 526.

Dr. J. A. Dudgeon: *The laboratory diagnosis of influenza.*—Influenza is an infection of the respiratory epithelium caused by a virus which is essentially pneumotropic and which is characterized by the recurrence of epidemics at frequent intervals throughout the world. During one such epidemic in this country in 1933, Wilson Smith, Andrewes and Laidlaw (1933) were able to show that a transmissible infection could be produced in ferrets following the intranasal inoculation of a filtrate from an early case of influenza. This was the first evidence that the causative organism of influenza was a virus and since that time strains have been isolated in many different parts of the world. So far, two antigenically distinct strains have been isolated from typical epidemics of influenza: influenza virus A, forming one large group (similar antigenically to the original strain isolated in 1933) and influenza virus B, the other distinct group first isolated seven years ago in the U.S.A. by Francis (1940) and independently by Magill (1940). These two viruses produce very much the same clinical picture of influenza, though they are distinct in their antigenic structure. As a rule virus B infections tend to be less virulent than those caused by the A virus.

The clinical diagnosis of influenza during an epidemic presents little difficulty, but the laboratory can provide useful information as to the type of infection, whether A or B, and in the case of sporadic influenza may be the only means of reaching a diagnosis from the other causes of upper respiratory infection.

There are two main methods of investigating influenza in the laboratory: (1) The direct method, which depends upon the isolation of the virus from throat washings of typical cases. (2) The indirect method, which depends upon the fact that infection is followed by a rise in serum antibody, which can be measured in several ways.

Direct method: Isolation of virus.—(*a*) *Ferret inoculation:* This is the classical method by which the virus was first isolated. The typical response to inoculation in a ferret is an acute upper respiratory infection accompanied by a varying degree of pyrexia, usually biphasic in type but often showing only a single peak, and followed by complete recovery of the ferret with the development of an immunity to further inoculation with the same virus. In recent years this typical picture of influenza in the ferret has not always been produced in the laboratory and the response in the ferret has been extremely variable. There may be a complete lack of symptoms, with practically no pyrexia, yet the serum antibody of the ferret may be markedly raised. More often there is a monophasic type of pyrexia with rapid recovery. This response in the ferret tends to vary with the pathogenicity of the virus for man. On the whole, virus B strains produce very few symptoms in the ferret and are not enhanced by passage, as is the case with A strains (Dudgeon *et al.*, 1946). Ferret inoculation thus has its limitations as a means of virus isolation and has to be carried out in specially equipped laboratories to exclude the risk of accidentally infecting the ferrets, which are to be used for virus isolation, with influenza and other viruses.

(*b*) *Developing chick embryo. Amniotic inoculation:* Burnet (1940) showed that the influenza virus could be adapted to growth in the amniotic sac of the developing chick embryo and that the virus could subsequently be recovered from the amniotic fluid, tracheal fluid and embryonic lungs. This method has opened up a new line of approach to the problem of influenza for this new medium, in which the virus will multiply, is not only economical and easy to handle, but devoid of latent viruses. Great progress has been made in the last few years in the development of this method until now it has become an extremely sensitive method of virus isolation.

The method adopted at the National Institute for Medical Research is that suggested by Beveridge and Burnet (1946). By the addition of antibacterial substances to the throat washing, filtration through a gradocol membrane is not necessary, the subsequent loss of virus is avoided and the maximum amount of virus allowed to come into contact with the respiratory epithelium. Throat washings containing 25% serum broth in saline are lightly centrifuged and are then inoculated direct into the amniotic cavity of 13-day chick embryos. Each egg receives 0·25 ml. throat washing and penicillin (100 units per ml.) and in addition 0·1 ml. of 5% sodium sulphamerazine. At least five eggs are inoculated with each washing as only a percentage become infected on primary passage. After a further four days' incubation all surviving eggs are chilled in the ice-box and are then tested for the presence of virus. For this purpose, use is made of the phenomenon described by Hirst (1941) and independently by McClelland and Hare (1941) who showed that the influenza virus would cause agglutination of fowl red cells, thus providing a useful laboratory test for the presence of the virus. Burnet and Bull (1943) showed that the influenza A virus on primary isolation would agglutinate guinea-pig (or other mammalian) red cells to a higher titre than it would fowl cells; this they called the O-phase ("Original"). After passage, however, the ratio changed and fowl red cells were agglutinated to a higher titre; this was named the D-phase ("Derivative"). This change in ratio is referred to as the O-D variation. It is therefore necessary to test primary amniotic fluids with both species of red cells. This phenomenon of the O-D variation is not shown by the B virus.

This method is an extremely sensitive one for virus isolation and virus typing and is comparatively easy to carry out once the technical details have been mastered.

Indirect method: Titration of serum antibody.—(*a*) *Neutralizing antibody:* The result of infection with influenza is a rise in both neutralizing and complement-fixing antibodies in the serum. This can best be determined by measuring the rise in serum antibody between an acute and convalescent sample of serum. The determination of the antibody level of a single specimen of serum is of little value in the test for neutralizing antibodies as it does not take into account past clinical and subclinical infections. The most convenient method of measuring the neutralizing antibody in serum is that described by Hirst (1941). The test is based on the fact that the agglutination of fowl red cells by the influenza virus can be inhibited by serum and the agglutinin-inhibition level of the serum determined. The modification of Hirst's original method described by Salk (1944) has many practical advantages. A fourfold rise in antibody between an acute and convalescent sample of serum has until recently been regarded as indicative of infection, but in carrying out a large series of these tests during two epidemics, one is impressed by the large number of sera from typical cases of influenza which only show a twofold rise, or, in a few cases, no rise in antibody. There are several technical difficulties associated with these red cell agglutination tests but on the whole they do provide a valuable guide to the diagnosis of influenza and also reflect the incidence of infection in a community.

(*b*) *Complement fixation:* There is an increase also in the complement-fixing antibody as a result of infection. Hoyle and Fairbrother (1937) have described a method of carrying out this test using the soluble antigen of influenza prepared from mouse lung, which gives a result in many cases comparable to the neutralization method (Hoyle, 1945). The advances made in recent years in the study of influenza are essentially practical and the methods described can be carried out in most laboratories with advantage to our knowledge of epidemic influenza.

requires three days before a report can be made. The detection of virus antigen in vesicle fluid or crusts by the complement-fixation technique is a highly specific test for variola-vaccinia antigen and gives reliable results if sufficient material is submitted for examination. The test for antibody is likely to be useful after the first week of illness and only if the patient has not recently been vaccinated.

REFERENCES

CRAIGIE, J., and WISHART, F. O. (1936) *Canad. publ. Hlth. J.*, 27, 371.
DOWNIE, A. W. (1946) *Monthly Bull. Min. Hlth. and Emerg. Publ. Hlth. Lab. Serv.*, 5, 114.
——, and DUMBELL, K. R. (1947*a*) *Lancet* (i), 550; (1947*b*) *J. Path. Bact.*, 59, 189.
IRONS, J. V., BOHLS, S. W., COOK, E. B. M., and MURPHY, J. N. (1941) *Amer. J. Hyg.*, 33 B, 50.
ROOYEN, C. E. VAN, and ILLINGWORTH, R. S. (1944) *Brit. med. J.* (ii), 526.

Dr. J. A. Dudgeon: *The laboratory diagnosis of influenza.*—Influenza is an infection of the respiratory epithelium caused by a virus which is essentially pneumotropic and which is characterized by the recurrence of epidemics at frequent intervals throughout the world. During one such epidemic in this country in 1933, Wilson Smith, Andrewes and Laidlaw (1933) were able to show that a transmissible infection could be produced in ferrets following the intranasal inoculation of a filtrate from an early case of influenza. This was the first evidence that the causative organism of influenza was a virus and since that time strains have been isolated in many different parts of the world. So far, two antigenically distinct strains have been isolated from typical epidemics of influenza: influenza virus A, forming one large group (similar antigenically to the original strain isolated in 1933) and influenza virus B, the other distinct group first isolated seven years ago in the U.S.A. by Francis (1940) and independently by Magill (1940). These two viruses produce very much the same clinical picture of influenza, though they are distinct in their antigenic structure. As a rule virus B infections tend to be less virulent than those caused by the A virus.

The clinical diagnosis of influenza during an epidemic presents little difficulty, but the laboratory can provide useful information as to the type of infection, whether A or B, and in the case of sporadic influenza may be the only means of reaching a diagnosis from the other causes of upper respiratory infection.

There are two main methods of investigating influenza in the laboratory: (1) The direct method, which depends upon the isolation of the virus from throat washings of typical cases. (2) The indirect method, which depends upon the fact that infection is followed by a rise in serum antibody, which can be measured in several ways.

Direct method: Isolation of virus.—(*a*) *Ferret inoculation:* This is the classical method by which the virus was first isolated. The typical response to inoculation in a ferret is an acute upper respiratory infection accompanied by a varying degree of pyrexia, usually biphasic in type but often showing only a single peak, and followed by complete recovery of the ferret with the development of an immunity to further inoculation with the same virus. In recent years this typical picture of influenza in the ferret has not always been produced in the laboratory and the response in the ferret has been extremely variable. There may be a complete lack of symptoms, with practically no pyrexia, yet the serum antibody of the ferret may be markedly raised. More often there is a monophasic type of pyrexia with rapid recovery. This response in the ferret tends to vary with the pathogenicity of the virus for man. On the whole, virus B strains produce very few symptoms in the ferret and are not enhanced by passage, as is the case with A strains (Dudgeon *et al.*, 1946). Ferret inoculation thus has its limitations as a means of virus isolation and has to be carried out in specially equipped laboratories to exclude the risk of accidentally infecting the ferrets, which are to be used for virus isolation, with influenza and other viruses.

(*b*) *Developing chick embryo. Amniotic inoculation:* Burnet (1940) showed that the influenza virus could be adapted to growth in the amniotic sac of the developing chick embryo and that the virus could subsequently be recovered from the amniotic

the urethra in the male or on the mucosa of the vulva, vagina or cervix in the female; it can occur more rarely about the anus or in the rectal mucosa, on the finger or in the mouth. Infection spreads by lymphatics to the nearest lymph glands and those most commonly involved are the inguinal. These may soften and break down and in the pus the virus can, at times, be demonstrated microscopically.

ISOLATION OF VIRUS BY ANIMAL OR EGG INOCULATION

Although microscopy is of value in the diagnosis of these infections its usefulness has definite limitations and it should never replace the attempt to isolate and identify the virus.

Psittacosis: In human cases of psittacosis the virus may be sought in the blood during the first few days of disease or later, in those cases where the lungs are involved, in the sputum or in material obtained by lung puncture. Both the incubated egg and the mouse are suitable for the isolation of psittacosis virus. If blood is the material to be examined it should be injected into mice intraperitoneally using as large an inoculum as possible. Sputum or lung puncture material, suspended in the least quantity of diluent (broth; saline; phosphate buffer) to provide an inoculum which can be injected through a reasonably fine needle, is used for the inoculation of mice by the peritoneal and nasal routes. It is important to employ the latter route since pigeon strains of psittacosis virus usually produce an inapparent infection in mice when injected intraperitoneally. Where bacteria are present in the material—and this applies particularly to sputum—filtration should be avoided if possible since it reduces the amount of virus, and the mice should be protected against the bacteria by the simultaneous injection of sulphathiazole to which psittacosis virus is usually insusceptible. I say "usually insusceptible" since contrary to the opinion of most workers, I have seen two cases of human psittacosis which appeared to respond to sulphapyridine and one to sulphathiazole. The inoculated mice should be observed for a month and any showing signs of illness killed, examined for signs of infection such as pneumonic consolidation in the nasally inoculated mice or enlargement of the spleen and peritonitis in those receiving the material by the peritoneal route. Should the lesions observed not appear to be of bacterial origin passage should be made to further mice with suspensions of lung or spleen respectively. Even in the absence of any signs of illness some of the mice should be killed after ten or twelve days and passage made in order to unmask a possible subclinical infection. This virus takes in the incubated hen's egg by practically any route, though for primary inoculation with material possibly containing some bacteria inoculation of the chorio-allantois would be the method of choice since this membrane is better able to deal with these bacteria than is the yolk sac. Some ten- to twelve-day eggs might, therefore, be inoculated in parallel with the mice.

Lymphogranuloma venereum: Pus from a bubo, preferably an unopened one, should be used for the inoculation of mice intracerebrally and four- to five-day eggs into the yolk sac. Should the pus contain bacterial secondary invaders it is sometimes possible to select the virus by injecting a suspension of the pus intradermally in the thigh of a guinea-pig and removing the inguinal glands on the same side two to three days later. A suspension of these glands, if culturally sterile, is then used for the inoculation of mice and eggs. One gets the impression from the literature that the isolation of this virus is a relatively easy matter, but my own experience does not confirm this. Material from three cases during the last year was inoculated into mice with a completely negative result in two, whilst from the third the strain obtained was lost after the third mouse passage. I understand that others in this country have had no better success than I.

The identification of strains of virus isolated from suspected cases of psittacosis or lymphogranuloma is made on the size and staining properties (Castaneda positive) of the virus and the infectivity for the mouse by the nasal, peritoneal and cerebral routes, these facts being considered in relation to the type of material examined and

REFERENCES

Beveridge, W. I. B., Burnet, F. M. (1946) *Spec. Rep. Ser. med. Res. Coun., Lond.* No. 256.
Burnet, F. M. (1940) *Aust. J. exp. Biol. med. Sci.*, 18, 353.
——, Bull, D. R. (1943) *Aust. J. exp. Biol. med. Sci.*, 21, 55.
Dudgeon, J. A., *et al.* (1946) *Lancet* (ii), 627.
Francis, T. (1940) *Science*, 92, 405.
Hirst, G. K. (1941) *Science*, 94, 22.
Hoyle, L. (1945) *J. Hyg.*, 44, 170.
——, Fairbrother, R. W. (1937) *Brit. J. exp. Path.*, 18, 425.
McClelland, L., Hare, R. (1941) *Canad. Publ. Hlth. J.*, 32, 530.
Magill, T. P. (1940) *Proc. Soc. exp. Biol. N.Y.*, 45, 162.
Salk, J. (1944) *J. Immunol.*, 49, 87.
Smith, W., Andrewes, C. H., Laidlaw, P. P. (1933) *Lancet* (ii), 66.

Professor S. P. Bedson: *Psittacosis-lymphogranuloma group.*—The viruses of the psittacosis-lymphogranuloma group belong to a larger group which includes, in addition, the viruses of trachoma, inclusion conjunctivitis or inclusion blennorrhœa, mouse pneumonitis of Nigg and Eaton and cat pneumonia of Baker. They are distinguished from other viruses by the possession in common of certain characters:

(1) Large size; their smallest forms are from 150 to 250 mμ in diameter.

(2) They stain more readily than other viruses and they can also be stained differentially by the method of Castaneda or Macchiavello, enabling them to be distinguished readily from particulate matter of a non-virus nature and from other viruses which do not stain by these methods.

(3) When multiplying they undergo a regular sequence of morphological change.

(4) Their cytoplasmic colonies or inclusions contain little inclusion material which is basophilic and its scantiness makes it possible readily to discern the structure of the inclusion.

(5) They contain thymonucleic acid unlike other viruses (Lépine and Sautter, 1946).

MICROSCOPY

It follows from this that microscopy should be of some service in the laboratory investigation of disease due to the psittacosis-lymphogranuloma group of viruses. Not that the microscope enables one to differentiate between these viruses because, of course, they look much the same, but it often makes it possible to say whether or not a virus of this group is present, and this information, coupled with the clinical data and knowledge of the source of the material, permits, if not the identification of the virus, at least a shrewd guess as to its identity.

Psittacosis infections.—Psittacosis is primarily a disease of birds. At one time it was thought that only psittacine birds were naturally affected, but we now know that the disease may occur in other species of birds. It has been observed in various species of finch, in fulmar petrels, in pigeons and in the domestic fowl and all these have been shown to be the source of human infections. Some authorities would distinguish between the strains of psittacosis virus occurring in these different bird species. Pigeon and fowl strains are sometimes referred to as ornithosis virus and though it is true that pigeon strains do differ in some respects from psittacine strains, it is too early yet to say whether these differences are sufficiently great to warrant different specific status. Man contracts infection usually by inhaling infective particles provided by dried droppings, and when clinically obvious the disease may take the form of a pyrexia without any signs of localization or accompanied by varying degrees of lung involvement. Although it may at times be possible to demonstrate the virus microscopically in sputum and lung puncture material this can hardly be recommended as a fruitful diagnostic procedure. In the case of infection of birds—and evidence of this may often be sought in connexion with the investigation of human cases of psittacosis—direct microscopy of smears made from the enlarged spleens or infected air sacs may often enable a rapid diagnosis.

Lymphogranuloma venereum.—Infection with this virus appears to be peculiar to man. Infection is spread by contact which in the main is venereal. The inconspicuous primary lesion usually occurs on the glans penis or in the anterior part of

the urethra in the male or on the mucosa of the vulva, vagina or cervix in the female; it can occur more rarely about the anus or in the rectal mucosa, on the finger or in the mouth. Infection spreads by lymphatics to the nearest lymph glands and those most commonly involved are the inguinal. These may soften and break down and in the pus the virus can, at times, be demonstrated microscopically.

ISOLATION OF VIRUS BY ANIMAL OR EGG INOCULATION

Although microscopy is of value in the diagnosis of these infections its usefulness has definite limitations and it should never replace the attempt to isolate and identify the virus.

Psittacosis: In human cases of psittacosis the virus may be sought in the blood during the first few days of disease or later, in those cases where the lungs are involved, in the sputum or in material obtained by lung puncture. Both the incubated egg and the mouse are suitable for the isolation of psittacosis virus. If blood is the material to be examined it should be injected into mice intraperitoneally using as large an inoculum as possible. Sputum or lung puncture material, suspended in the least quantity of diluent (broth; saline; phosphate buffer) to provide an inoculum which can be injected through a reasonably fine needle, is used for the inoculation of mice by the peritoneal and nasal routes. It is important to employ the latter route since pigeon strains of psittacosis virus usually produce an inapparent infection in mice when injected intraperitoneally. Where bacteria are present in the material—and this applies particularly to sputum—filtration should be avoided if possible since it reduces the amount of virus, and the mice should be protected against the bacteria by the simultaneous injection of sulphathiazole to which psittacosis virus is usually insusceptible. I say "usually insusceptible" since contrary to the opinion of most workers, I have seen two cases of human psittacosis which appeared to respond to sulphapyridine and one to sulphathiazole. The inoculated mice should be observed for a month and any showing signs of illness killed, examined for signs of infection such as pneumonic consolidation in the nasally inoculated mice or enlargement of the spleen and peritonitis in those receiving the material by the peritoneal route. Should the lesions observed not appear to be of bacterial origin passage should be made to further mice with suspensions of lung or spleen respectively. Even in the absence of any signs of illness some of the mice should be killed after ten or twelve days and passage made in order to unmask a possible subclinical infection. This virus takes in the incubated hen's egg by practically any route, though for primary inoculation with material possibly containing some bacteria inoculation of the chorio-allantois would be the method of choice since this membrane is better able to deal with these bacteria than is the yolk sac. Some ten- to twelve-day eggs might, therefore, be inoculated in parallel with the mice.

Lymphogranuloma venereum: Pus from a bubo, preferably an unopened one, should be used for the inoculation of mice intracerebrally and four- to five-day eggs into the yolk sac. Should the pus contain bacterial secondary invaders it is sometimes possible to select the virus by injecting a suspension of the pus intradermally in the thigh of a guinea-pig and removing the inguinal glands on the same side two to three days later. A suspension of these glands, if culturally sterile, is then used for the inoculation of mice and eggs. One gets the impression from the literature that the isolation of this virus is a relatively easy matter, but my own experience does not confirm this. Material from three cases during the last year was inoculated into mice with a completely negative result in two, whilst from the third the strain obtained was lost after the third mouse passage. I understand that others in this country have had no better success than I.

The identification of strains of virus isolated from suspected cases of psittacosis or lymphogranuloma is made on the size and staining properties (Castaneda positive) of the virus and the infectivity for the mouse by the nasal, peritoneal and cerebral routes, these facts being considered in relation to the type of material examined and

REFERENCES

BEVERIDGE, W. I. B., BURNET, F. M. (1946) *Spec. Rep. Ser. med. Res. Coun., Lond.* No. 256.
BURNET, F. M. (1940) *Aust. J. exp. Biol. med. Sci.*, 18, 353.
——, BULL, D. R. (1943) *Aust. J. exp. Biol. med. Sci.*, 21, 55.
DUDGEON, J. A., *et al.* (1946) *Lancet* (ii), 627.
FRANCIS, T. (1940) *Science*, 92, 405.
HIRST, G. K. (1941) *Science*, 94, 22.
HOYLE, L. (1945) *J. Hyg.*, 44, 170.
——, FAIRBROTHER, R. W. (1937) *Brit. J. exp. Path.*, 18, 425.
MCCLELLAND, L., HARE, R. (1941) *Canad. Publ. Hlth. J.*, 32, 530.
MAGILL, T. P. (1940) *Proc. Soc. exp. Biol. N.Y.*, 45, 162.
SALK, J. (1944) *J. Immunol.*, 49, 87.
SMITH, W., ANDREWES, C. H., LAIDLAW, P. P. (1933) *Lancet* (ii), 66.

Professor S. P. Bedson: *Psittacosis-lymphogranuloma group.*—The viruses of the psittacosis-lymphogranuloma group belong to a larger group which includes, in addition, the viruses of trachoma, inclusion conjunctivitis or inclusion blennorrhœa, mouse pneumonitis of Nigg and Eaton and cat pneumonia of Baker. They are distinguished from other viruses by the possession in common of certain characters:

(1) Large size; their smallest forms are from 150 to 250 mμ in diameter.

(2) They stain more readily than other viruses and they can also be stained differentially by the method of Castaneda or Macchiavello, enabling them to be distinguished readily from particulate matter of a non-virus nature and from other viruses which do not stain by these methods.

(3) When multiplying they undergo a regular sequence of morphological change.

(4) Their cytoplasmic colonies or inclusions contain little inclusion material which is basophilic and its scantiness makes it possible readily to discern the structure of the inclusion.

(5) They contain thymonucleic acid unlike other viruses (Lépine and Sautter, 1946).

MICROSCOPY

It follows from this that microscopy should be of some service in the laboratory investigation of disease due to the psittacosis-lymphogranuloma group of viruses. Not that the microscope enables one to differentiate between these viruses because, of course, they look much the same, but it often makes it possible to say whether or not a virus of this group is present, and this information, coupled with the clinical data and knowledge of the source of the material, permits, if not the identification of the virus, at least a shrewd guess as to its identity.

Psittacosis infections.—Psittacosis is primarily a disease of birds. At one time it was thought that only psittacine birds were naturally affected, but we now know that the disease may occur in other species of birds. It has been observed in various species of finch, in fulmar petrels, in pigeons and in the domestic fowl and all these have been shown to be the source of human infections. Some authorities would distinguish between the strains of psittacosis virus occurring in these different bird species. Pigeon and fowl strains are sometimes referred to as ornithosis virus and though it is true that pigeon strains do differ in some respects from psittacine strains, it is too early yet to say whether these differences are sufficiently great to warrant different specific status. Man contracts infection usually by inhaling infective particles provided by dried droppings, and when clinically obvious the disease may take the form of a pyrexia without any signs of localization or accompanied by varying degrees of lung involvement. Although it may at times be possible to demonstrate the virus microscopically in sputum and lung puncture material this can hardly be recommended as a fruitful diagnostic procedure. In the case of infection of birds—and evidence of this may often be sought in connexion with the investigation of human cases of psittacosis—direct microscopy of smears made from the enlarged spleens or infected air sacs may often enable a rapid diagnosis.

Lymphogranuloma venereum.—Infection with this virus appears to be peculiar to man. Infection is spread by contact which in the main is venereal. The inconspicuous primary lesion usually occurs on the glans penis or in the anterior part of

the urethra in the male or on the mucosa of the vulva, vagina or cervix in the female; it can occur more rarely about the anus or in the rectal mucosa, on the finger or in the mouth. Infection spreads by lymphatics to the nearest lymph glands and those most commonly involved are the inguinal. These may soften and break down and in the pus the virus can, at times, be demonstrated microscopically.

ISOLATION OF VIRUS BY ANIMAL OR EGG INOCULATION

Although microscopy is of value in the diagnosis of these infections its usefulness has definite limitations and it should never replace the attempt to isolate and identify the virus.

Psittacosis: In human cases of psittacosis the virus may be sought in the blood during the first few days of disease or later, in those cases where the lungs are involved, in the sputum or in material obtained by lung puncture. Both the incubated egg and the mouse are suitable for the isolation of psittacosis virus. If blood is the material to be examined it should be injected into mice intraperitoneally using as large an inoculum as possible. Sputum or lung puncture material, suspended in the least quantity of diluent (broth; saline; phosphate buffer) to provide an inoculum which can be injected through a reasonably fine needle, is used for the inoculation of mice by the peritoneal and nasal routes. It is important to employ the latter route since pigeon strains of psittacosis virus usually produce an inapparent infection in mice when injected intraperitoneally. Where bacteria are present in the material—and this applies particularly to sputum—filtration should be avoided if possible since it reduces the amount of virus, and the mice should be protected against the bacteria by the simultaneous injection of sulphathiazole to which psittacosis virus is usually insusceptible. I say "usually insusceptible" since contrary to the opinion of most workers, I have seen two cases of human psittacosis which appeared to respond to sulphapyridine and one to sulphathiazole. The inoculated mice should be observed for a month and any showing signs of illness killed, examined for signs of infection such as pneumonic consolidation in the nasally inoculated mice or enlargement of the spleen and peritonitis in those receiving the material by the peritoneal route. Should the lesions observed not appear to be of bacterial origin passage should be made to further mice with suspensions of lung or spleen respectively. Even in the absence of any signs of illness some of the mice should be killed after ten or twelve days and passage made in order to unmask a possible subclinical infection. This virus takes in the incubated hen's egg by practically any route, though for primary inoculation with material possibly containing some bacteria inoculation of the chorio-allantois would be the method of choice since this membrane is better able to deal with these bacteria than is the yolk sac. Some ten- to twelve-day eggs might, therefore, be inoculated in parallel with the mice.

Lymphogranuloma venereum: Pus from a bubo, preferably an unopened one, should be used for the inoculation of mice intracerebrally and four- to five-day eggs into the yolk sac. Should the pus contain bacterial secondary invaders it is sometimes possible to select the virus by injecting a suspension of the pus intradermally in the thigh of a guinea-pig and removing the inguinal glands on the same side two to three days later. A suspension of these glands, if culturally sterile, is then used for the inoculation of mice and eggs. One gets the impression from the literature that the isolation of this virus is a relatively easy matter, but my own experience does not confirm this. Material from three cases during the last year was inoculated into mice with a completely negative result in two, whilst from the third the strain obtained was lost after the third mouse passage. I understand that others in this country have had no better success than I.

The identification of strains of virus isolated from suspected cases of psittacosis or lymphogranuloma is made on the size and staining properties (Castaneda positive) of the virus and the infectivity for the mouse by the nasal, peritoneal and cerebral routes, these facts being considered in relation to the type of material examined and

REFERENCES

BEVERIDGE, W. I. B., BURNET, F. M. (1946) *Spec. Rep. Ser. med. Res. Coun., Lond.* No. 256.
BURNET, F. M. (1940) *Aust. J. exp. Biol. med. Sci.*, 18, 353.
——, BULL, D. R. (1943) *Aust. J. exp. Biol. med. Sci.*, 21, 55.
DUDGEON, J. A., *et al.* (1946) *Lancet* (ii), 627.
FRANCIS, T. (1940) *Science*, 92, 405.
HIRST, G. K. (1941) *Science*, 94, 22.
HOYLE, L. (1945) *J. Hyg.*, 44, 170.
——, FAIRBROTHER, R. W. (1937) *Brit. J. exp. Path.*, 18, 425.
MCCLELLAND, L., HARE, R. (1941) *Canad. Publ. Hlth. J.*, 32, 530.
MAGILL, T. P. (1940) *Proc. Soc. exp. Biol. N.Y.*, 45, 162.
SALK, J. (1944) *J. Immunol.*, 49, 87.
SMITH, W., ANDREWES, C. H., LAIDLAW, P. P. (1933) *Lancet* (ii), 66.

Professor S. P. Bedson: *Psittacosis-lymphogranuloma group.*—The viruses of the psittacosis-lymphogranuloma group belong to a larger group which includes, in addition, the viruses of trachoma, inclusion conjunctivitis or inclusion blennorrhœa, mouse pneumonitis of Nigg and Eaton and cat pneumonia of Baker. They are distinguished from other viruses by the possession in common of certain characters:

(1) Large size; their smallest forms are from 150 to 250 $m\mu$ in diameter.

(2) They stain more readily than other viruses and they can also be stained differentially by the method of Castaneda or Macchiavello, enabling them to be distinguished readily from particulate matter of a non-virus nature and from other viruses which do not stain by these methods.

(3) When multiplying they undergo a regular sequence of morphological change.

(4) Their cytoplasmic colonies or inclusions contain little inclusion material which is basophilic and its scantiness makes it possible readily to discern the structure of the inclusion.

(5) They contain thymonucleic acid unlike other viruses (Lépine and Sautter, 1946).

MICROSCOPY

It follows from this that microscopy should be of some service in the laboratory investigation of disease due to the psittacosis-lymphogranuloma group of viruses. Not that the microscope enables one to differentiate between these viruses because, of course, they look much the same, but it often makes it possible to say whether or not a virus of this group is present, and this information, coupled with the clinical data and knowledge of the source of the material, permits, if not the identification of the virus, at least a shrewd guess as to its identity.

Psittacosis infections.—Psittacosis is primarily a disease of birds. At one time it was thought that only psittacine birds were naturally affected, but we now know that the disease may occur in other species of birds. It has been observed in various species of finch, in fulmar petrels, in pigeons and in the domestic fowl and all these have been shown to be the source of human infections. Some authorities would distinguish between the strains of psittacosis virus occurring in these different bird species. Pigeon and fowl strains are sometimes referred to as ornithosis virus and though it is true that pigeon strains do differ in some respects from psittacine strains, it is too early yet to say whether these differences are sufficiently great to warrant different specific status. Man contracts infection usually by inhaling infective particles provided by dried droppings, and when clinically obvious the disease may take the form of a pyrexia without any signs of localization or accompanied by varying degrees of lung involvement. Although it may at times be possible to demonstrate the virus microscopically in sputum and lung puncture material this can hardly be recommended as a fruitful diagnostic procedure. In the case of infection of birds—and evidence of this may often be sought in connexion with the investigation of human cases of psittacosis—direct microscopy of smears made from the enlarged spleens or infected air sacs may often enable a rapid diagnosis.

Lymphogranuloma venereum.—Infection with this virus appears to be peculiar to man. Infection is spread by contact which in the main is venereal. The inconspicuous primary lesion usually occurs on the glans penis or in the anterior part of

essential in a clinically equivocal case. The work of Rake and Eaton and their colleagues during the last few years is even more upsetting to our preconceptions. Rake, Eaton and Shaffer (1941) have shown that sera from cases of psittacosis, lymphogranuloma and atypical pneumonia fix complement equally well with psittacosis, meningopneumonitis (ornithosis) and lymphogranuloma antigens and what is of equal importance, that cases of atypical pneumonia due to psittacosis virus may give a positive Frei test. This evidence of antigenic sharing between these viruses has been further supported by cross-immunity experiments in animals (Eaton, Martin and Beck, 1942; Beck, Eaton and O'Donnell, 1944). My own experience confirms this. Sera from cases diagnosed clinically as lymphogranuloma and giving a positive Frei test have fixed complement just as well with a psittacosis antigen as with one prepared from lymphogranuloma virus, though in the few cases in which I have made an intradermal test with the psittacosis antigen in addition to the Frei test with lygranum, the skin tests have not always shown the concordance of the serological tests. The implications of this work are obvious. These serological tests in disease due to viruses of the psittacosis-lymphogranuloma group are not virus-specific but only group-specific and their interpretation must invariably be made in the light of the clinical and epidemiological evidence. There is even a suggestion that this sharing of antigens extends to other Castaneda-positive viruses and that antibody-fixing complement with psittacosis and L.G.V. antigens may occur in trachoma and infections with the related virus of inclusion conjunctivitis (Rake, Shaffer and Thygeson, 1942). The few observations I have made have not confirmed this. The Frei test, too, loses its specificity and must be read in conjunction with the clinical and serological findings. The whole position is a little confused and in my opinion it will remain so until we have a more exact understanding of the antigenic relationship of these viruses.

REFERENCES

BECK, M. D., EATON, M. D., and O'DONNELL, R. (1944) *J. exp. Med.*, 79, 65.
BEDSON, S. P. (1935) *Lancet* (ii), 1277.
—— (1936) *Brit. J. exp. Path.*, 17, 109.
—— (1937) *Lancet* (ii), 1477.
COUTTS, W. E., and PONCE, T. (1935) *J. Lab. clin. Med.*, 20, 629.
EATON, M. D. (1943) *Calif. West. Med.*, 59, 8.
——, BECK, M. D., and PEARSON, H. E. (1941) *J. exp. Med.*, 73, 641.
——, MARTIN, W. P., and BECK, M. D. (1942) *J. exp. Med.*, 75, 21.
FAVOUR, C. B. (1943) *Amer. J. med. Sci.*, 205, 162.
HECHT, H. (1935) *Wien. klin. Wschr.*, 48, 1389.
LANDAU, H. D. (1946) *J. Path. Bact.*, 58, 568.
LÉPINE, P., and SAUTTER, V. (1946) *Ann. Inst. Past.*, 72, 174.
MERRIL, M. H. (1936) *J. Immunol.*, 30, 169.
MEYER, K. F., EDDIE, B., and YANAMURA, H. (1939) *Proc. Soc. exp. Biol. N.Y.*, 41, 173.
——, ——, —— (1942) *Proc. Soc. exp. Biol. N.Y.*, 49, 609.
RAKE, G., EATON, M. D., and SHAFFER, M. F. (1941) *Proc. Soc. exp. Biol. N.Y.*, 48, 528.
——, SHAFFER, M. F., and THYGESON, P. (1942) *Proc. Soc. exp. Biol. N.Y.*, 49, 545.
SHAFFER, M. F., RAKE, G., and GRACE, A. W. (1942) *Amer. J. Syph.*, 26, 271.
SMADEL, J. E. (1943) *J. Clin. Invest.*, 22, 57.

Dr. F. O. MacCallum: *Neurotropic viruses.*—Our present knowledge indicates that infection by the known neurotropic viruses occurs comparatively rarely in this country, but interest in them has greatly increased in recent years. There are, in addition, a considerable number of cases of benign meningitis, meningo-encephalitis, encephalitis and myelitis, which are presumably of virus origin. Thus, there are two interesting problems: on the one hand to determine the possible reasons for the limitation of spread in epidemic form of recognized diseases such as acute anterior poliomyelitis and, on the other, to identify the causative agents of the group of presumed neurotropic virus infections.

The first of these problems does not concern us here; as to the second, since the clinical picture does not serve to differentiate virus infections of the C.N.S., the differential diagnosis within each group depends on the aid of the laboratory. The exceptions are rabies, and poliomyelitis, where, usually, the laboratory is only the clinical history of the case supplying it. There are other tests that can be applied, such as infectivity for the pigeon and cross-immunity tests in mice or hamsters, but these are the concern of the expert.

SEROLOGICAL DIAGNOSIS

The isolation and identification of these viruses naturally take time, and valuable and necessary though this type of laboratory investigation may be, its findings are only of retrospective interest as far as the clinician is concerned. It is for this reason that the indirect method of laboratory diagnosis of this disease has been developed despite the fact that the answer provided by the demonstration of antibody in the patient's serum is of less value than isolation and identification of the virus. Specific antibodies are developed with considerable regularity in these infections and their presence can be detected most satisfactorily by the complement-fixation test. It is true that the agglutination reaction, even slide agglutination, can be used for this purpose but as Merril has shown (1936), the complement-fixation test is the more delicate and therefore of greater value where, as is the case with viruses, an antigen of high concentration is difficult to obtain. Some twelve years ago (Bedson, 1935) we started using the complement-fixation test at the London Hospital for the diagnosis of psittacosis. At first the antigen used was a crude suspension of virulent mouse spleen, but when it was found that a partially purified suspension of virus heated to 100° C. was even more satisfactory (Bedson, 1936) this safer antigen was employed. The results obtained with this test appeared to accord well with the clinical, epidemiological and other laboratory findings (Bedson, 1937) and confirmation of this has been forthcoming from America (Meyer, Eddie and Yanamura, 1939). More recently the complement-fixation test has been used in the diagnosis of lymphogranuloma venereum and found to be of service (Hecht, 1935; Coutts and Ponce, 1935; Shaffer, Rake and Grace, 1942; Landau, 1946). Much of the earlier work in this field was based on the assumption that these reactions were specific and that a single observation showing a reasonably high titre of antibody was diagnostic, but a more extended use of these tests and a study of the relationship of the viruses of the psittacosis-lymphogranuloma group have shown these assumptions to be unwarranted. One has always held that for serological evidence of active infection to be acceptable there should be a material excursion in the titre of the antibodies in question, either a rising titre in the active stage of the disease or a falling one in the convalescence, preferably the former. Extended use of the psittacosis complement-fixation test has shown that it is no exception to the rule. This has emerged clearly from the serological investigations of the virus syndrome, primary atypical pneumonia, made during the war. A proportion, roughly about 10%, of these cases are caused by viruses of the psittacosis group. In a series of 45 sporadic cases investigated by Smadel (1943) in eastern urban populations of the United States, 9 showed serological evidence of being due to psittacosis virus and this virus was isolated from the sputum in one; in another case in which the C.F.T. was not done the virus was isolated from the lungs post mortem. In this country (Bedson unpublished) 9 of 120 cases had either a very high or a rising titre of antibody for psittacosis virus. Other workers in America (Eaton, Beck and Pearson, 1941; Meyer, Eddie and Yanamura, 1942; Eaton, 1943; Favour, 1943) have produced evidence that viruses of the psittacosis group are concerned in the causation of atypical pneumonia. Smadel (1943) commenting on the use of the complement-fixation test in the investigation of this condition gives it as his opinion that a rise of not less than fourfold in the antibody titre is necessary if one is to conclude that the presence of antibody denotes active infection, and with this view I would certainly concur. My more limited experience of the complement-fixation test in lymphogranuloma leads me to a similar conclusion; though a single observation showing a high titre in a clinically acceptable case is good confirmatory evidence, a rising titre of antibody is better and is quite found in the Americas have not been seen in this country in animals or man, but as equine encephalomyelitis has occurred in all the States of the eastern coast of U.S.A. in recent years, one cannot ignore the possibility of such an infection. Infection with the viruses of Japanese B. encephalitis and Russian spring-summer (tick-borne) encephalitis can probably be disregarded, though the latter appears to be closely related immunologically to louping-ill, which is found in sheep in Scotland and is said to have been isolated in Russia.

Louping-ill is the only one of the known virus encephalitides under suspicion at the moment. This virus infection of sheep, transmitted by the tick *Ixodes ricinus*, is, as far as is known, confined to Scotland and northern England. Infection in man is only known to have occurred in laboratory workers or in veterinarians who have done post-mortem examinations on infected sheep. A serological survey is now in progress to determine whether unrecognized infection is more widespread than is realized, as was found to be the case with Rift-Valley fever.

Though poliomyelitis has never become the serious disease that it is in Australia, Canada, and U.S.A., it is an endemic infection in this country and provides a very interesting problem for study. As can be seen from the table, the virus of poliomyelitis can be isolated from the nasopharyngeal secretions and intestinal contents during life and from the central nervous system as well as some other tissues, of fatal cases. The virus has *not* been isolated from the cerebrospinal fluid and has been detected in the blood only very rarely. Unfortunately, small laboratory animals are not susceptible to most strains of the virus, and it is necessary to use monkeys for the original isolation. This makes routine laboratory diagnosis of this disease impracticable in England at the present time. The immunological relationship of different strains is not yet clear, but certain strains which have been adapted to mice can be used for serological surveys of immunity. We are using such a strain for these tests now and are attempting to adapt to rodents a strain isolated by inoculation of rhesus monkeys from a fatal human case in London in June 1946.

The largest group of cases which needs investigation is that of benign lymphocytic or aseptic meningitis, of which a certain proportion are caused by the known virus of lymphocytic choriomeningitis (L.C.M.), but the majority are of undetermined origin. L.C.M. virus has been isolated on a number of occasions in the U.S.A., and neutralizing antibodies were found in the sera of about 10% of 1,000 individuals giving no history of disease of the central nervous system. The virus of L.C.M. has been found to exist as a latent infection in some mouse colonies, and has been isolated from mice trapped in houses where human cases of L.C.M. have occurred. In England, the position seems to be somewhat different. The virus has been isolated from man on only about 12 occasions. In several instances, where there appears to have been undoubted isolation of the virus from man by inoculation into clean stocks of mice and guinea-pigs, neither neutralizing nor complement-fixing antibodies could be detected in the patients' serum in the convalescent stage. It is hoped that further study will reveal more exactly the part that L.C.M. virus plays in benign aseptic meningitis in this country.

The virus of L.C.M. may be isolated from the blood in the febrile, influenza-like, pre-meningeal phase, but the disease will not be recognized in this stage, except where a number of cases occur in one focus within a short period. The virus is present in the cerebrospinal fluid for a comparatively short space of time during the acute stage of the meningitis. Whole blood (2·0 to 10·0 c.c.) and C.S.F. (5·0 to 10·0 c.c.) should be collected in the febrile and meningeal stages, for isolation of virus and clotted blood (3·0 to 10·0 c.c.) in the acute stage and four to six weeks later for antibody estimations. The amount of blood and C.S.F. collected will, of course, depend on the circumstances, but it is obvious that the larger the sample for study, the greater the chance of carrying out satisfactory tests.

needed to verify the clinical diagnosis, although sporadic cases of poliomyelitis may be simulated by other virus infections, e.g. lymphocytic choriomeningitis.

The laboratory diagnosis of infections with neurotropic viruses entails the application of methods similar to those used in the diagnosis of any other infectious disease. In the acute stage, attempts are made to isolate the causative agent by growth in appropriate culture media, e.g. the developing hen's egg, and experimental animals ranging from mouse to chimpanzee. In the convalescent period, various serological tests are used to detect the presence of specific antibodies, e.g. neutralizing and complement-fixing antibodies, agglutinins and precipitins. No attempt will be made here to describe in detail the methods and constituents of the tests used in each case, but rather to make a general statement indicating the type of test used and the necessary materials to be collected from the patient for laboratory diagnosis.

In the detection of virus in the acute stage, the most important point is the proper collection, storage and transport of material to be examined. If in doubt, it will always be most helpful for all concerned if the laboratory which is to carry out the investigations is consulted beforehand. Many of these viruses are comparatively heat labile as soon as they are removed from their natural host, and it is essential that all such material should be kept at temperatures below +4° C. immediately they are obtained from the patient and until received at the laboratory for diagnosis.

Many laboratories now possess refrigerators maintained at a temperature of −20° C. which is most satisfactory; otherwise small specimens may be frozen in the coil of the refrigerator. Specimens should be packed in ice for transport and dispatched to the diagnostic laboratory by the most rapid method of delivery. The exception to this is blood serum for serological tests, which may be sent by post. For complement-fixation tests in particular, it is essential to have clean sterile, non-hæmolysed serum, so that when possible, the serum should be removed from the clot before dispatching it.

SITES FROM WHICH VIRUSES MAY BE ISOLATED AND APPROPRIATE SEROLOGICAL TESTS

Virus	Central nervous system	Cerebro-spinal fluid	Blood	Naso-pharynx	Intestine	Com-plement fixation	Neutral-ization
Rabies	+	−	−	+	−	‡	*
Poliomyelitis	+	−	rarely	+	+	‡	?value
St. Louis encephalitis	+	rarely	rarely	−	−	+	+
Western equine encephalomyelitis	+	rarely	rarely	−	−	+	+
Eastern equine encephalomyelitis	+	rarely	rarely	−	−	+	+
Venezuelan equine encephalomyelitis	+	−	+	+	−	+	+
Japanese B. encephalitis	+	+	+	−	−	+	+
Russian spring-summer encephalitis	+	+	+	−	−	+	+
Louping-ill	+	rarely	rarely	−	−	+	+
Lymphocytic choriomeningitis	*	+	+	+	−	+	+
Mumps	*	+	−	+	−	+	+
Herpes	+	+	−	−	−	‡	?value
Lymphogranuloma venereum	−	+	+	−	−	+	+

* Not tested so far. ‡ No test.

In the table are listed the sites from which virus has been isolated, or the appropriate serological tests in the more common neurotropic virus diseases of man, and some neurotropic virus diseases of animals, which are known to have affected workers experimenting with them, e.g. louping-ill. As far as we know, we are concerned with comparatively few of these recognized infections in Great Britain.

Rabies is no longer a problem, though occasionally cases occur in individuals who have been bitten by a rabid animal abroad and who develop the disease after returning to England. Two such cases from Greece and India have recently occurred in London and confirmation of the clinical diagnosis was obtained by infecting mice, guinea-pigs and rabbits with suspension of the brain which had been placed in 50% glycerol-saline at post-mortem.

St. Louis encephalitis and the various types of equine encephalomyelitis which are found in the Americas have not been seen in this country in animals or man, but as equine encephalomyelitis has occurred in all the States of the eastern coast of U.S.A. in recent years, one cannot ignore the possibility of such an infection. Infection with the viruses of Japanese B. encephalitis and Russian spring-summer (tick-borne) encephalitis can probably be disregarded, though the latter appears to be closely related immunologically to louping-ill, which is found in sheep in Scotland and is said to have been isolated in Russia.

Louping-ill is the only one of the known virus encephalitides under suspicion at the moment. This virus infection of sheep, transmitted by the tick *Ixodes ricinus*, is, as far as is known, confined to Scotland and northern England. Infection in man is only known to have occurred in laboratory workers or in veterinarians who have done post-mortem examinations on infected sheep. A serological survey is now in progress to determine whether unrecognized infection is more widespread than is realized, as was found to be the case with Rift-Valley fever.

Though poliomyelitis has never become the serious disease that it is in Australia, Canada, and U.S.A., it is an endemic infection in this country and provides a very interesting problem for study. As can be seen from the table, the virus of poliomyelitis can be isolated from the nasopharyngeal secretions and intestinal contents during life and from the central nervous system as well as some other tissues, of fatal cases. The virus has *not* been isolated from the cerebrospinal fluid and has been detected in the blood only very rarely. Unfortunately, small laboratory animals are not susceptible to most strains of the virus, and it is necessary to use monkeys for the original isolation. This makes routine laboratory diagnosis of this disease impracticable in England at the present time. The immunological relationship of different strains is not yet clear, but certain strains which have been adapted to mice can be used for serological surveys of immunity. We are using such a strain for these tests now and are attempting to adapt to rodents a strain isolated by inoculation of rhesus monkeys from a fatal human case in London in June 1946.

The largest group of cases which needs investigation is that of benign lymphocytic or aseptic meningitis, of which a certain proportion are caused by the known virus of lymphocytic choriomeningitis (L.C.M.), but the majority are of undetermined origin. L.C.M. virus has been isolated on a number of occasions in the U.S.A., and neutralizing antibodies were found in the sera of about 10% of 1,000 individuals giving no history of disease of the central nervous system. The virus of L.C.M. has been found to exist as a latent infection in some mouse colonies, and has been isolated from mice trapped in houses where human cases of L.C.M. have occurred. In England, the position seems to be somewhat different. The virus has been isolated from man on only about 12 occasions. In several instances, where there appears to have been undoubted isolation of the virus from man by inoculation into clean stocks of mice and guinea-pigs, neither neutralizing nor complement-fixing antibodies could be detected in the patients' serum in the convalescent stage. It is hoped that further study will reveal more exactly the part that L.C.M. virus plays in benign aseptic meningitis in this country.

The virus of L.C.M. may be isolated from the blood in the febrile, influenza-like, pre-meningeal phase, but the disease will not be recognized in this stage, except where a number of cases occur in one focus within a short period. The virus is present in the cerebrospinal fluid for a comparatively short space of time during the acute stage of the meningitis. Whole blood (2·0 to 10·0 c.c.) and C.S.F. (5·0 to 10·0 c.c.) should be collected in the febrile and meningeal stages, for isolation of virus and clotted blood (3·0 to 10·0 c.c.) in the acute stage and four to six weeks later for antibody estimations. The amount of blood and C.S.F. collected will, of course, depend on the circumstances, but it is obvious that the larger the sample for study, the greater the chance of carrying out satisfactory tests.

needed to verify the clinical diagnosis, although sporadic cases of poliomyelitis may be simulated by other virus infections, e.g. lymphocytic choriomeningitis.

The laboratory diagnosis of infections with neurotropic viruses entails the application of methods similar to those used in the diagnosis of any other infectious disease. In the acute stage, attempts are made to isolate the causative agent by growth in appropriate culture media, e.g. the developing hen's egg, and experimental animals ranging from mouse to chimpanzee. In the convalescent period, various serological tests are used to detect the presence of specific antibodies, e.g. neutralizing and complement-fixing antibodies, agglutinins and precipitins. No attempt will be made here to describe in detail the methods and constituents of the tests used in each case, but rather to make a general statement indicating the type of test used and the necessary materials to be collected from the patient for laboratory diagnosis.

In the detection of virus in the acute stage, the most important point is the proper collection, storage and transport of material to be examined. If in doubt, it will always be most helpful for all concerned if the laboratory which is to carry out the investigations is consulted beforehand. Many of these viruses are comparatively heat labile as soon as they are removed from their natural host, and it is essential that all such material should be kept at temperatures below +4° C. immediately they are obtained from the patient and until received at the laboratory for diagnosis.

Many laboratories now possess refrigerators maintained at a temperature of −20° C. which is most satisfactory; otherwise small specimens may be frozen in the coil of the refrigerator. Specimens should be packed in ice for transport and dispatched to the diagnostic laboratory by the most rapid method of delivery. The exception to this is blood serum for serological tests, which may be sent by post. For complement-fixation tests in particular, it is essential to have clean sterile, non-hæmolysed serum, so that when possible, the serum should be removed from the clot before dispatching it.

SITES FROM WHICH VIRUSES MAY BE ISOLATED AND APPROPRIATE SEROLOGICAL TESTS

Virus	Central nervous system	Cerebro-spinal fluid	Blood	Naso-pharynx	Intestine	Complement fixation	Neutralization
Rabies	+	−	−	+	−	‡	*
Poliomyelitis	+	−	rarely	+	+	‡	?value
St. Louis encephalitis	+	rarely	rarely	−	−	+	+
Western equine encephalomyelitis..	+	rarely	rarely	−	−	+	+
Eastern equine encephalomyelitis ..	+	rarely	rarely	−	−	+	+
Venezuelan equine encephalomyelitis..	+	−	+	+	−	+	+
Japanese B. encephalitis	+	+	+	−	−	+	+
Russian spring-summer encephalitis	+	+	+	−	−	+	+
Louping-ill	+	rarely	rarely	−	−	+	+
Lymphocytic choriomeningitis ..	*	+	+	+	−	+	+
Mumps	*	+	−	+	−	+	+
Herpes	+	+	−	−	−	‡	?value
Lymphogranuloma venereum ..	−	+	+	−	−	+	+

* Not tested so far. ‡ No test.

In the table are listed the sites from which virus has been isolated, or the appropriate serological tests in the more common neurotropic virus diseases of man, and some neurotropic virus diseases of animals, which are known to have affected workers experimenting with them, e.g. louping-ill. As far as we know, we are concerned with comparatively few of these recognized infections in Great Britain.

Rabies is no longer a problem, though occasionally cases occur in individuals who have been bitten by a rabid animal abroad and who develop the disease after returning to England. Two such cases from Greece and India have recently occurred in London and confirmation of the clinical diagnosis was obtained by infecting mice, guinea-pigs and rabbits with suspension of the brain which had been placed in 50% glycerol-saline at post-mortem.

St. Louis encephalitis and the various types of equine encephalomyelitis which are

Section of Radiology

President—Whately Davidson, M.D., F.R.C.P., F.F.R.

[*February* 21, 1947]

Carcinoma of the Thyroid

By J. M. Graham, P.R.C.S.Ed., and R. McWhirter, F.R.C.S.Ed.

The object of this communication is to discuss some of the facts associated with malignant disease of the thyroid gland with special reference to the results of treatment. Our observations are based upon a series of 144 unselected cases which have been drawn mainly from the south-east of Scotland and have been admitted to the Royal Infirmary, Edinburgh. The cases are representative of an area in which simple goitre is not endemic but occurs only sporadically.

Sex incidence.—Of the total number of patients 31 were males and 113 were females. These figures, which show a ratio of 1 male to 3·6 females, may be compared with those of a corresponding series of cases of simple goitre, which were operated on, in which the incidence was 1 male to 9 females.

Age.—The average age of the cases was 59·75 years. The youngest patient was 18 and the oldest was 93.

Histological Classification

The diagnosis of malignant disease was confirmed by histological examination in 97 of the cases. In the remaining 47 cases it was made on clinical grounds alone.

As the histological reports were made originally by several pathologists, we considered it would be advantageous to have the slides reviewed by one experienced authority. We are indebted to Professor Drennan, Professor of Pathology at Edinburgh University, for undertaking this work and for classifying the cases on a uniform basis. His opinion has enabled us to eliminate a few cases in which the original diagnosis of malignant disease was not confirmed, and a review of the subsequent history of these rejected cases has supported the correctness of the final histological report. Some of the slides of the early cases were not available for inspection, and in all 79 of the 97 cases have been classified by Professor Drennan.

In 34 (23%) of the present series there was a history of a previous goitre. In most classifications it is usual to include these cases in a separate group referred to under the descriptive term "malignant adenoma". This arrangement has not been retained as the degree of malignancy and the histological appearances in such cases vary within wide limits. Some of the tumours, commencing in a fœtal adenoma, are relatively slow-growing and well-differentiated, while in other cases the tumours are rapidly growing, highly malignant and composed of undifferentiated cells. For the purpose of this investigation, therefore, the cases of malignant adenoma have been grouped according to the histological type.

All cases, whether beginning in an adenoma or not, have been subdivided into three histological groups:

Recent studies in various centres have suggested that in an epidemic of mumps there may be a number of cases which never show any signs or symptoms of parotitis, but have meningitic symptoms and an increase of cells in the C.S.F. It is obvious that such cases may occur apart from an epidemic and so provide a proportion of cases of benign aseptic meningitis. The virus of mumps has been isolated from the C.S.F. as well as the saliva by inoculation into the parotid gland of rhesus monkeys, and into the developing hen's egg. However, the simplest method of diagnosis is the examination of acute and convalescent sera for antibody using either the complement-fixation or fowl red cell agglutination tests.

The virus of herpes simplex has been isolated from the C.S.F. of a suspected case of lymphocytic choriomeningitis and from the central nervous system of four cases of fatal encephalitis in the U.S.A. We isolated this virus at the Wellcome Institute in 1940 from tissues of a fatal case of encephalitis sent us by Major C. H. Stuart-Harris, R.A.M.C. The patient was a soldier who died in France before Dunkirk and though the tissues for virus isolation survived the journey, the tissues prepared for histological examination were destroyed. Thus, proof of origin of the virus was lacking. The part that herpes simplex virus plays in non-fatal infections of the central nervous system will be difficult to determine by serological tests because of the large number of individuals who carry the virus and have antibodies to it in their blood, but changes in antibody titre during the acute and convalescent stages of a suspected case would be significant.

Involvement of the central nervous system in cases of infection with the virus of lymphogranuloma venereum (L.G.V.) has been reported. Virus has been isolated from the C.S.F. by inoculation of animals. The apparently small number of infections with this virus reported in this country suggest, however, that this complication will seldom be seen.

It is probable that there are numerous other viruses still to be isolated from the large group of cases of benign meningitis, encephalitis and encephalomyelitis. In all these cases, the method of attack is essentially the same; collection of whole blood and C.S.F. in the acute stage of the illness and acute and convalescent sera if the case is not fatal.

In fatal cases, pieces of the central nervous system and any other organ which appears to be affected are collected with aseptic precautions and placed in sterile containers. These tissues may be preserved in this manner at 4° C. or lower, but if 50% glycerol-saline is available, it is advisable to add this to the specimens in order to prevent growth of any bacteria that may be present, and also support survival of the virus if it is not possible to store at temperatures below +4° C. At the same time, similar pieces of tissues are placed in fixative for histological examination.

Summary.—The isolation and identification of a neurotropic virus require close co-operation between the clinician and laboratory in the collection of specimens.

All specimens for examination, e.g. nasopharyngeal washings, whole blood, C.S.F., intestinal contents, and post-mortem tissues should be kept at temperatures below 4° C. after collection from the patient. Whole blood and cerebrospinal fluid should be collected in the acute stages of the illness for virus isolation and blood serum in the acute and convalescent stages for antibody studies.

Infection with the known neurotropic viruses appears to be uncommon in England, with the exception of poliomyelitis virus. It is hoped that a more intensive investigation of suspected cases will reveal previously unidentified viruses and further information concerning known infections, such as those of the viruses of lymphocytic choriomeningitis, poliomyelitis and mumps.

Section of Radiology

President—Whately Davidson, M.D., F.R.C.P., F.F.R.

[*February* 21, 1947]

Carcinoma of the Thyroid

By J. M. Graham, P.R.C.S.Ed., and R. McWhirter, F.R.C.S.Ed.

The object of this communication is to discuss some of the facts associated with malignant disease of the thyroid gland with special reference to the results of treatment. Our observations are based upon a series of 144 unselected cases which have been drawn mainly from the south-east of Scotland and have been admitted to the Royal Infirmary, Edinburgh. The cases are representative of an area in which simple goitre is not endemic but occurs only sporadically.

Sex incidence.—Of the total number of patients 31 were males and 113 were females. These figures, which show a ratio of 1 male to 3·6 females, may be compared with those of a corresponding series of cases of simple goitre, which were operated on, in which the incidence was 1 male to 9 females.

Age.—The average age of the cases was 59·75 years. The youngest patient was 18 and the oldest was 93.

Histological Classification

The diagnosis of malignant disease was confirmed by histological examination in 97 of the cases. In the remaining 47 cases it was made on clinical grounds alone.

As the histological reports were made originally by several pathologists, we considered it would be advantageous to have the slides reviewed by one experienced authority. We are indebted to Professor Drennan, Professor of Pathology at Edinburgh University, for undertaking this work and for classifying the cases on a uniform basis. His opinion has enabled us to eliminate a few cases in which the original diagnosis of malignant disease was not confirmed, and a review of the subsequent history of these rejected cases has supported the correctness of the final histological report. Some of the slides of the early cases were not available for inspection, and in all 79 of the 97 cases have been classified by Professor Drennan.

In 34 (23%) of the present series there was a history of a previous goitre. In most classifications it is usual to include these cases in a separate group referred to under the descriptive term "malignant adenoma". This arrangement has not been retained as the degree of malignancy and the histological appearances in such cases vary within wide limits. Some of the tumours, commencing in a fœtal adenoma, are relatively slow-growing and well-differentiated, while in other cases the tumours are rapidly growing, highly malignant and composed of undifferentiated cells. For the purpose of this investigation, therefore, the cases of malignant adenoma have been grouped according to the histological type.

All cases, whether beginning in an adenoma or not, have been subdivided into three histological groups:

(1) Adenocarcinoma	18 cases	23%
(2) Papillary Adenocarcinoma ..	13 cases	16%
(3) Undifferentiated Carcinoma	48 cases	61%

Squamous metaplasia may occasionally occur but as a rule this involves only a portion of the tumour which can therefore still be classified into one or other of the above types.

The same rule was adopted where portions of the tumour had a sarcomatous appearance due to the cells having a spindle shape. We agree with Ewing that sarcoma of the thyroid must be exceedingly rare for when large sections are examined it is often possible to trace continuity between the spindle cells and areas which are typically carcinomatous.

A scirrhous reaction is rare in thyroid carcinoma and in this connexion it may be of interest to draw attention to the fact that bony metastases in thyroid cancer are nearly always osteolytic, i.e. as in the soft tissues so in bone the tumour cells fail to excite a reaction to their presence.

(1) *Adenocarcinoma.*—The cases in this group are those in which the cells retain a definite acinous formation which varies in the individual case in the degree of deviation from the normal. In some cases areas of undifferentiated carcinoma are present, but these cases are included within this group when the acinous structure is obvious throughout most of the sections. Variations therefore in the degree of malignancy and the rapidity of growth are observed. The average duration of the malignant disease when the patient first came to hospital was eleven months, and it is characteristic of this group that the tumour grows relatively slowly. The signs of malignancy are obvious when the capsule is invaded and the growth is attached to the adjacent structures. Secondary involvement of the lymph glands was present in 3 of the 18 cases; it was only observed after the tumour had become fixed. Invasion of the vascular spaces is comparatively frequent, and distant metastases were present in 2 of the cases when first seen, and developed later in a considerable number. It was observed that the secondary growths tended to show a greater degree of differentiation than the primary tumours.

(2) *Papillary Adenocarcinoma.*—The history of the cases before and after treatment indicates that this is the most slowly growing and least malignant type of thyroid tumour. The average duration of the disease in the cases in this group before coming to hospital was thirty-eight months, and we have records of cases in which the growth has persisted or recurred over a period of twenty years.

The tumour may be comparatively cystic or apparently solid, depending on the extent to which the cystic spaces are filled with papilliferous tissue. It may reach to a large size before the clinical picture of a fixed, malignant goitre is presented. The signs of malignancy remain localized in the neck as a rule, and there is little tendency to spread by the blood-stream; distant metastases were observed only in one case. The cervical lymph glands were already invaded in 3 of the cases when first seen, and further evidence of the tendency to spread by the lymph stream in this type of carcinoma appeared subsequently, after operation or radiotherapy, in a considerable proportion of the cases.

The histological picture shows a greater degree of differentiation than in other types of carcinoma of the thyroid. The papillary processes are lined by a single layer of cuboidal or columnar epithelium, or in some cases by more than one layer. Compared with the simple type of papilloma the papillary processes have less connective tissue and proportionately more epithelium. Occasionally syncytial masses may be seen or local areas where the epithelial cells are escaping into the stroma or invading the capsule. In the absence of these signs it may be difficult to decide whether a papillary type of tumour is benign or malignant.

The following case may be quoted as an example of this type of carcinoma:—

Doris W., aged 18. Several enlarged glands were noticed on the left side of the neck. They were regarded as tuberculous by her medical man, but no improvement followed sunlight treatment. When she was admitted to hospital eleven months later the left lobe of the thyroid was enlarged to approximately twice its normal size, and was nodular in outline, firm and almost hard in consistence. Five or six enlarged glands were felt beneath the sternomastoid and in the posterior triangle of the neck on the same side. At operation on 9.10.42 the left lobe was found to be adherent to the trachea, but there was no sign of infiltration. The entire left lobe of the thyroid and the isthmus were removed, together with the internal jugular vein to which the glands were adherent, from the level of the tonsillar gland to a short distance above the clavicle. Several glands were also cleared from the posterior triangle. Subsequently the patient received a course of X-ray therapy. She has so far remained free of recurrence.

The entire left lobe was found to be replaced by a greyish-white fleshy tissue, and the cut surface of the lymph glands had a similar appearance. Microscopically the sections from the thyroid lobe showed a highly differentiated papillary adenocarcinoma with more cellular areas in which the papillary structure was absent. The glands were almost entirely replaced by a similar type of carcinoma, but here and there the structure of a lymph gland could be recognized at the periphery.

There seemed no doubt in this case that the tumour was a papillary adenocarcinoma of the thyroid with secondary widespread involvement of the cervical glands on the same side. It could not therefore be confused with the type of case referred to by Crile in which he describes the occurrence of multiple papillary adenomata arising in lateral aberrant thyroid rests, with or without a similar type of papillary tumour in the thyroid gland, which he attributes to multicentric primary growths in aberrant thyroid tissue.

(3) *Undifferentiated Carcinoma.*—This is the most malignant form of goitre. It was the commonest type in our series, occurring in 48 cases (61 %). It usually presents the typical clinical features of malignant disease at an early stage. With few exceptions the tumour grows rapidly and is inoperable within a few months or even weeks of its first appearance. Tumours of this type soon become fixed to the trachea, œsophagus and adjacent structures, and pressure symptoms are common. Secondary involvement of the lymph glands was present in 12 of the 48 cases. Distant metastases were found in 8 of the cases at the time of their first examination. Frequently death occurs before metastases, due to blood-spread, have time to become clinically obvious.

The microscopic picture usually found is that of masses or sheets of uniform spheroidal or polygonal cells with little or no stroma. However this uniformity of cell type is not always present and a varying degree of pleomorphism may occur. In the more extreme examples typical multinucleated giant cells may be observed in extensive portions of the tumour.

The following is an example of an exceptional case of undifferentiated carcinoma in which the rate of growth was extremely slow:

Robert A., aged 57 years. A swelling in the left lobe of the thyroid had been present for several years. During a period of six months it had slowly increased in size. The tumour was recognized as a solitary adenoma, firm in consistence and about 6 cm. in diameter. It appeared to be partly fixed to the deeper structures. The tumour was removed by enucleation-resection on 10.3.31. Both macroscopically and microscopically it showed the characteristics of a fœtal adenoma of long standing. There was evidence, however, of more active growth towards the surface, where the cells were spheroidal in type without acinous formation.

Five years later a local recurrence in the neck was removed, and this showed the structure of an undifferentiated carcinoma with little evidence of active mitosis.

In 1939 metastases appeared in the lungs. The patient remained in comparatively good health, although subsequent X-ray photographs showed considerable extension of the metastatic deposits in the chest, until shortly before his death in 1946.

CARCINOMA OF ABERRANT THYROID TISSUE

Three of the tumours in our series had their origin in aberrant thyroid tissue. Most aberrant thyroid tumours show a papillary structure, whether benign or malignant. The cases now referred to illustrate the three main histological types which carcinoma of the thyroid may assume.

(1) *Adenocarcinoma of lateral aberrant thyroid.*—William C., aged 33. The tumour was situated in the right side of the neck opposite the angle of the mandible. It had slowly increased in size and even at the end of three years was only 4×3 cm. Histologically it had the structure of an adeno-

carcinoma which was well encapsulated, and was obviously of a low grade of malignancy. It was removed in 1944, and the patient subsequently received X-ray treatment. There has been no recurrence.

(2) *Papillary adenocarcinoma of lateral aberrant thyroid.*—Job B., aged 56. A tumour on the right side of the neck was first noticed in 1923. When removed in 1924 it formed a large, encapsuled and partly cystic growth which lay beneath the sternomastoid and in the supraclavicular fossa. It was adherent to the internal jugular and subclavian veins. It was not connected with the thyroid gland. A recurrence appeared two years later, but the patient was not seen until 1936. The tumour then formed a large fixed mass in the lower part of the neck on the right side, extending into the superior mediastinum and into both axillæ. No improvement followed X-ray therapy.

The original tumour had the structure of a papillary adenoma. Sections made from the growth thirteen years after it had first been noticed showed the typical appearance of a papillary adenocarcinoma. The papillæ had more evidence of epithelial activity than formerly, and there were areas also of undifferentiated carcinoma.

In spite of the extent of the growth, the patient's general condition was good, and he was successfully operated on in two stages for simple hypertrophy of the prostate. He died five months later without signs of metastases elsewhere.

The case illustrates the slow rate of growth and the local nature of this type of malignant disease.

(3) *Undifferentiated carcinoma in a lingual thyroid.*—Mrs. I., aged 47. In childhood a thyroglossal cyst had been removed from the mid-line of the neck. A lingual thyroid was noted at the level of the hyoid in 1931. As the patient suffered no inconvenience operation was not considered. When she reported to hospital five years later the swelling at the back of the tongue was much increased in size and caused considerable discomfort in swallowing. A firm, enlarged gland was present in the right tonsillar region. The growth in the tongue was firm in consistence and was more extensive on the right side. Although not ulcerated its malignant nature was apparent. On X-ray examination of the neck the tumour could be seen projecting backwards in the lateral view, and the usual shadow of the thyroid gland was absent from its normal position.

A course of X-ray treatment was given. The enlarged gland disappeared, and the tumour in the tongue was reduced in size. Ten months later the patient returned in poor condition. Several indurated masses could be felt in the lateral walls of the pharynx and in the anterior pillar of the fauces. An X-ray examination of the chest showed gross metastases in the lungs. The patient died in hospital, and at the post-mortem a shrunken carcinoma with considerable fibrosis was found in the back of the tongue. Sections from the tongue and from the metastases showed an undifferentiated form of carcinoma similar to that commonly seen in the thyroid.

DIFFERENTIAL DIAGNOSIS

In many cases the nature of the condition is only too obvious. The chief problems of diagnosis are related to the early stages. We have had no case in our series in which the diagnosis was made purely on histological grounds. The diagnosis was obvious or at least suspected clinically in all but one case in which, however, the specimen after operation showed macroscopically the characteristics of a carcinoma. In this respect the series differs materially from many recorded, especially in American literature, in which a high proportion of the cases are examples of early malignant adenoma showing only microscopically the evidence of malignancy. Few, if any, cases of such a nature can have been missed in our series, as we have no record of a case, in which the histological diagnosis of simple adenoma was originally made, returning later with metastases or local recurrence.

The appearance of a nodular goitre in a patient approaching middle age, recent increase in the size of a goitre, or alteration in its consistence or outline should be regarded with suspicion. Fixation of the swelling to the trachea while the thyroid still moves freely on swallowing is one of the earliest signs to appear. X-ray examination of the neck will show the position of the trachea. Forward displacement of the trachea with antero-posterior narrowing of the lumen is much more suggestive of carcinoma than of simple goitre. A barium swallow in cases with dysphagia frequently shows narrowing of the œsophagus such as is rarely seen in simple goitre.

A calcified adenoma or nodular goitre may be very hard, but the presence of even extensive calcification does not exclude carcinoma. Evidence of calcification has been present in several of our cases.

An old nodular goitre which has undergone degenerative changes with varying amounts of fibrosis and lymphocytic infiltration may closely simulate malignant disease. Such cases merge into true Riedel's or ligneous thyroiditis, which in our experience is much rarer than malignant disease.

Riedel's thyroiditis.—The chief characteristic feature of ligneous thyroiditis is the densely hard consistence. The swelling may be limited to one lobe or may involve the whole of the thyroid gland. It is usually of limited size, smooth or only slightly nodular in outline and, although it may be fixed, of slower growth than the type of carcinoma with which it is likely to be confused. The swelling, which may be tender, is not associated with enlargement of the lymph glands.

Hashimoto's thyroiditis or lymphogenous goitre has in the past frequently been mistaken for malignant disease, but a careful consideration of the facts of the case will usually enable it to be distinguished. It occurs in women and the whole gland is obviously enlarged to a moderate extent. It is smooth in outline and firm rather than hard in consistence. The gland outline is exceptionally well-defined and mobilization of the lobes, should operation be undertaken, is unusually easy. Although with increasing experience most cases of Hashimoto's thyroiditis can be recognized, there are exceptions in which the gland is firmer or more fixed than usual, but the nature of the goitre should be apparent at operation or if a biopsy is done.

Syphilitic thyroiditis.—We have seen two cases of gummatous disease and one of interstitial fibrosis due to syphilis in which malignant disease was simulated. In two of the cases the history and other signs suggested the diagnosis, and the condition was relieved by antisyphilitic treatment. In the remaining case an emergency operation was required. The patient, a male, aged 17, was admitted suffering from dysphagia and severe dyspnœa associated with a swelling in the region of the thyroid which had first been noticed ten weeks previously. The thyroid was irregularly enlarged and firm, with a fixed, tumour-like mass in the region of the isthmus. A pre-operative diagnosis of carcinoma of the thyroid was made, and appeared to be confirmed at the time of operation by the fact that the tissue had infiltrated as well as compressed the trachea. The tumour and a portion of the anterior wall of the trachea were removed, and the patient was left with a tracheotomy. Sections of the tissue on examination showed the typical changes of a gumma, and the Wassermann was strongly positive. The patient showed none of the ordinary signs of congenital syphilis from which he was suffering.

Hæmorrhage into a thyroid cyst.—We have seen several cases of rapid enlargement of a thyroid cyst due to hæmorrhage which were readily recognized as such. In one case, however—that of an elderly woman with a large cyst—the hæmorrhage had evidently been recurrent and gradual. When admitted as an emergency case she was suffering from dyspnœa which had prevented her from lying down for three weeks and which had become extreme. The swelling and tension in the neck were such that there seemed little doubt that the symptoms were due to a rapidly growing carcinoma. Operation, reluctantly undertaken, led to the happiest result.

Secondary carcinoma of the thyroid.—The fact that malignant goitre may be due to direct spread from an epithelioma of the pharynx or cervical œsophagus requires emphasis. The dysphagia present may be regarded as due to the thyroid enlargement. Direct examination, therefore, may be necessary to exclude a primary growth in the gullet.

TREATMENT OF CARCINOMA OF THE THYROID

Factors affecting the survival rate.—Before discussing the results obtained attention must be drawn to two points which have an important bearing on the survival rate.

(1) The review differs from most publications in that it is not confined to cases actually treated but includes all cases referred to a large general hospital. In 53% of the cases either no treatment at all was given or such treatment as was possible was purely palliative. It will be clear, therefore, that the survey is not limited to early operable cases.

(2) The series contains a high proportion of undifferentiated carcinomata. These cases constituted 61% of the total classified cases. Undifferentiated carcinomata are rapidly growing and are often inoperable by the time they are first seen. Actually it was found that 25% of them died within one month and 50% were dead within four months of the time when they first came to hospital.

The survival rate of cases not histologically proven.—33% of the cases were not histologically proven but as already noted many cases were advanced and in some of the rapidly growing tumours the patient's distress was so great and the necessity for treatment so urgent that it was considered inadvisable to subject the patient even to such a minor procedure as a biopsy. In a few such cases where a biopsy was attempted the trauma of exposing the tumour and the few days' delay in commencing treatment led to the death of the patient. As will be shown later many of these tumours respond rapidly to X-ray therapy and in a very short time there is no tumour tissue available for removal. The following table shows that, of the cases in which the diagnosis was established on clinical grounds alone, the survival rate was not higher than where the diagnosis was confirmed histologically.

TABLE I
HISTOLOGICALLY PROVEN

No. of Cases = 97 (67% of Total)

Years after treatment	Exposed to risk	q_x*	Survival rate
0	83·5	·5868	100%
1	31·5	·2540	41·32%
2	19	·0526	30·82%
3	16	·0625	29·20%
4	12	·0833	27·38%
5			25·10%

TABLE II
NOT HISTOLOGICALLY PROVEN
No. of Cases = 47 (33% of Total)

Years after treatment	Exposed to risk	q_x*	Survival rate
0	45	·6667	100%
1	14	·1428	33·33%
2	12	·0000	28·57%
3	11	·0909	28·57%
4	8·5	·1176	25·97%
5			22·92%

*The "q_x" value is the probability or chance of any one patient dying in any particular year. The figures are obtained by the method of calculation suggested by Dr. Lewis-Fáning and they provide a more reliable indication of the results than those obtainable by more ordinary methods. It will be noted that the survival rate for each year is given in the last column.

The method of investigating the results.—In determining the best method of treatment the ideal approach to the problem would be to compare a series of cases treated by surgery alone with a comparable series treated by X-rays alone. Unfortunately this was not possible because surgical removal was confined to operable cases and only inoperable cases were treated by X-rays alone.

The problem of determining the most appropriate method of treatment had therefore to be approached in a more indirect manner. Two methods of investigation appeared to be worth considering:

(*a*) To ascertain the results according to the clinical extent of the disease.
(*b*) To ascertain the results according to the histological nature of the tumour.

(*a*) *The results according to the clinical extent of the disease.*—For the purposes of this paper the following clinical classification was adopted.

Operable: The primary tumour was either mobile or only slightly fixed to the adjacent tissues. If glands were present they must be mobile and confined to one side of the neck.

Inoperable: No distant metastases. All cases in which the primary tumour was extensively fixed to the adjacent tissues. Bilateral glands or fixed glands confined to the neck.

Inoperable: Distant metastases present. All cases with clinical or radiographic evidence of distant metastases.

Recurrent: All cases originally treated elsewhere and only referred when local recurrences or distant metastases had taken place.

TABLE III

TREATMENT METHODS USED

	Total	Radical Surgery with or without X-rays	Radical X-rays	Palliative treatment	No treatment
Operable	29	29	—	0	0
Inoperable: no distant metastases	84	0	39	37	8
Inoperable: distant metastases	24	0	0	16	8
Recurrent	7	0	0	6	1
Total	144	29	39	59	17
%	100%	20%	27%	41%	12%

All cases with distant metastases and all the recurrent cases are dead and need not be considered further.

Of the 29 operable cases all were fully treated and so far as could be ascertained at the time of the operation the tumour was apparently completely removed. Seven cases were treated by complete thyroidectomy and the remainder by subtotal thyroidectomy. There were no post-operative deaths. In 18 cases post-operative X-ray therapy was given. The five-year survival rate was 73% as is shown in Table IV.

TABLE IV

29 OPERABLE CASES (20% OF THE TOTAL)

Years after treatment	Exposed to risk	q_x	Survival rate
0	26	·2692	100
1	17·5	·0000	73·08%
2	14	·0000	73·08%
3	13	·0000	73·08%
4	11	·0000	73·08%
5			73·08%

Of the 11 cases alive at the end of five years, 4 had immediate post-operative X-ray therapy, and of the remaining 7 which were treated by surgery alone in the first place 4 recurred within five years and were then treated by X-rays. After five years a further 2 had recurrences treated by X-rays leaving only one symptom-free case treated by surgery alone.

Of the 84 inoperable cases without clinical or radiographic evidence of distant metastases it will be seen from Table III that 8 had no treatment at all and that 37 had only palliative treatment. In a number of cases surgical removal was attempted but had to be abandoned because of the extent of the disease. In spite of what has been said it will be seen from Table V that 16% of the cases were alive at the end of five years.

TABLE V

INOPERABLE. NO DISTANT METASTASES
No. of Cases = 84 (58% of Total)

Years after treatment	Exposed to risk	q_x	Survival rate
0	76	·6842	100%
1	22	·2727	31·58%
2	16	·1250	22·97%
3	12	·0000	20·10%
4	9·5	·2105	20·10%
5			15·87%

In only 39 of the 84 cases could the X-ray treatment be considered adequate, and of this more limited series 29% were alive at the end of five years.

TABLE VI

INOPERABLE. NO DISTANT METASTASES
RADICAL X-RAYS
No. of Cases = 39

Years after treatment	Exposed to risk	q_x	Survival rate
0	38	·5526	100%
1	16	·1250	44·74%
2	14	·1428	39·15%
3	10	·0000	33·56%
4	7·5	·1333	33·56%
5			29·09%

(*b*) *Results according to the histological type of tumour.*—In the following tables all cases whether treated or not are included. The numbers are small and the results must be accepted with caution until larger numbers have been treated.

Of the 18 cases of adenocarcinoma 46% were alive at the end of five years.

TABLE VII

ADENOCARCINOMA. ALL CASES HISTOLOGICALLY PROVEN
No. of Cases = 18

Years after treatment	Exposed to risk	q_x	Survival rate
0	15·5	·3871	100%
1	8	·2500	61·3%
2	4	·0000	46·0%
3	4	·0000	46·0%
4	2	·0000	46·0%
5			46·0%

Of the 13 cases of papillary adenocarcinoma 40% were alive at the end of five years.

TABLE VIII

PAPILLARY ADENOCARCINOMA. ALL CASES HISTOLOGICALLY PROVEN
No. of Cases = 13

Years after treatment	Exposed to risk	q_x	Survival rate
0	10·5	·1905	100%
1	8	·1250	80·95%
2	7	·1429	70·83%
3	6	·1667	60·71%
4	5	·2000	50·59%
5			40·47%

Both the adenocarcinomata and the papillary adenocarcinomata are as a rule slowly-growing tumours and untreated cases or incompletely treated cases may survive for more than five years. The efficacy of treatment could be ascertained more clearly in these cases by a study of the ten-year survival rate. In both groups of cases surgery and X-rays were employed in their treatment but surgery appeared to play the more important rôle.

In the undifferentiated tumours on the other hand, the five-year survival rate is a good guide to the value of treatment for they are nearly always very rapidly growing and hence rapidly fatal unless successfully treated. In spite of the fact that many are highly radiosensitive high five-year survival rates are not to be expected for these tumours disseminate early and widely and 80% were inoperable by the time they were first seen. The five-year survival rate of all cases was 14% and as no case treated by surgery alone survived for five years the results must be attributed to X-ray treatment.

TABLE IX

UNDIFFERENTIATED CARCINOMA. ALL CASES HISTOLOGICALLY PROVEN

No. of Cases = 48

Years after treatment	Exposed to risk	q	Survival rate
0	43·5	·7586	100%
1	10	·4000	24·14%
2	5	·0000	14·48%
3	4	·0000	14·48%
4	3	·0000	14·48%
5			14·48%

Mention has been made of the fact that many undifferentiated carcinomata are highly radiosensitive and indeed they are amongst the most radiosensitive tumours of the whole body. Their radiosensitivity may be compared with the medulloblastomata, the seminomata and with certain types of reticulum-cell sarcomata. The sensitive types respond far more rapidly to treatment than lymphogenous goitre and absolute proof that these sensitive cases were, in fact, malignant tumours has been ascertained beyond any doubt by the observance of metastases as well as by histological examination.

The undifferentiated carcinomata are often admitted to hospital as emergencies and must be treated forthwith or the patient will die. It is doubtful if the urgency of these cases and the value of X-rays in their treatment is fully appreciated by members of hospital staffs. Too often they are given morphia or an attempt is made to perform a tracheotomy. When treated by X-rays dramatic relief may be obtained in as short a time as twenty-four hours.

Conclusions from the Two Investigations.—From the foregoing analysis the following points emerge:

As might be expected the best results are obtained in the early (i.e. the operable) cases where surgical removal with or without post-operative X-ray therapy gives a satisfactory five-year survival rate. Unfortunately only 20% of the total cases were in this early category. The value of post-operative X-rays is difficult to assess in this group as the numbers are too small to permit of a more detailed analysis.

In the inoperable cases such surgical intervention as was undertaken was limited and amounted as a rule only to biopsy. In no case was all the tumour tissue removed. The five-year survival rate obtained must be credited to X-rays alone and the figures especially in the cases treated by X-rays show that X-rays have a definite and useful part to play in the treatment of thyroid carcinoma even when the tumour is completely inoperable.

Examination of the results according to the histological type of the tumour shows that the histological type is an important guide to the five-year survival rate and that better results are to be expected in the tumours showing some degree of differentiation.

The analysis, while of some value, does not clearly indicate the best method of treatment to be adopted, but in view of the obvious importance of the histological type of the tumour it was decided to carry this aspect of the investigation further.

THE RADIOSENSITIVITY OF THE DIFFERENT HISTOLOGICAL TYPES

In determining the radiosensitivity of the three histological subdivisions account was taken, in this analysis, only of the rate of response of the tumour tissue treated irrespective of whether the primary tumour itself or only a gland or metastatic deposit was being treated. If the tumour diminished rapidly in size it was regarded as radiosensitive and all other cases were placed in the radioresistant category. The survival rate was ignored because clearly a case might respond well in the treated area and yet die in a short time from some other known or unknown deposit.

In 19 cases where the X-ray treatment followed surgery it appeared possible that all the tumour tissue had been removed and these cases were, of course, excluded from the analysis. In a further 61 cases either no X-ray treatment was given or else the dosage was so low that no useful assessment could be made. In the remaining 64 cases sufficient dosage was given to the clinically obvious tumour to determine its sensitivity. The results are shown in Table X.

TABLE X

RADIOSENSITIVITY

Radiosensitivity Determined	64
? No Tissue to test Radiosensitivity	19
No treatment or palliative treatment	61
Total ..	144

	Adeno-carcinoma	Pap.adeno-carcinoma	Undiff. carcinoma	Type unknown	Total
Radiosensitive	0	0	11	17	28
Not radiosensitive	7	3	9	17	36
Total	7	3	20	34	64
%Radiosensitive	0%	0%	55%	50%	44%

Somewhat surprisingly it was found that all the tumours proving to be radiosensitive were in the completely undifferentiated category. The numbers of differentiated tumours are too small for the conclusion to be drawn that all differentiated tumours are radioresistant and clearly further observations require to be made.

The other interesting point is that all the undifferentiated tumours were not radiosensitive—in fact only 55% were radiosensitive. So far it has not been possible to distinguish these two types from one another by histological examination, thus recalling an observation made in a previous communication to this Society where it was shown that the radiosensitive and the radioresistant meningiomata cannot be distinguished from one another by means of histological examination. (*Proc. R. Soc. Med.*, 1946, 39, 673.)

However, other findings are of some help in distinguishing the radiosensitive group. The average duration of symptoms in the radiosensitive cases was 6·3 months and of the radioresistant cases sixteen months. Of the 28 radiosensitive cases only three had pre-existing adenomata and the tumour as a rule involved the gland diffusely, producing a smooth uniform enlargement of the whole gland.

It will be noted that of the 64 cases 44% were radiosensitive and therefore suitable for treatment by radiotherapy. The five year survival rate however is poor in these cases because of the early spread of cells to distant sites. Where death took place in a short period of time it was found that most of the patients died from metastases in the lungs. Because of the already high tendency of these tumours to spread to the lungs the greatest care must be taken not to carry out any procedure which may possibly increase this tendency to metastasize. It follows therefore if a tumour is possibly of the radiosensitive type that any attempt at surgical removal should not be made, for incomplete removal will almost certainly bring about dissemination of cells. Similarly, resort to tracheotomy in cases of severe dyspnœa is inadvisable, not only because this will only prolong life by a few days or weeks, but also because a tracheotomy under these conditions will so disturb the tumour that dissemination of cells is highly probable and because tracheotomy will interfere with the application of X-rays. These observations are further supported by the findings in other tumours, and the work done on breast carcinoma in Edinburgh suggests that spread of tumour cells by operation is not uncommon. In making this statement it will be appreciated that the remarks apply only to possibly radiosensitive tumours. Where tumours are likely to be insensitive considerable palliative relief may be obtained by the removal of as much of the tumour as possible and if the tumour is slowly growing this relief may last for a considerable time.

The table also shows clearly the value of the method of histological classification adopted and suggests that the older classifications which recognized the malignant adenoma as a subdivision might well be abandoned. As already indicated the malignant adenoma may consist of any of the three above types. It is a clinical term and gives no guide to the radiosensitivity of a tumour and therefore to the best method or combination of methods to be used.

INDICATIONS FOR OPERATION

Operation is indicated when there is a reasonable prospect of removing the tumour completely. If the growth is limited to part of a lobe the entire lobe should be removed with the isthmus. Limited fixation of the tumour does not exclude an operation on the same lines. When the nature of the goitre is uncertain at the operation it is better to remove the lobe rather than to do a partial resection. Extensive involvement of both lobes usually means that complete excision of the growth is impossible. A varying amount of the second lobe may, however, be removed. A complete thyroidectomy is rarely indicated.

If enlarged glands are present the case is usually inoperable. The presence of enlarged glands and of a slow-growing tumour of the thyroid suggesting a papillary adenocarcinoma is an indication for a radical operation including the removal of the affected thyroid lobe, even if it is adherent, and of the glands by a wide and thorough dissection.

In operable cases any signs of invasion of the superficial veins require a more extensive operation, including removal of the internal jugular vein together with the affected lobe with its veins intact, as suggested by Joll.

When the tumour is fixed and complete removal is regarded as impossible, a biopsy only is done. As already noted the incomplete removal of an undifferentiated and therefore usually highly malignant goitre is likely to be followed by extensive local recurrence and rapid dissemination to distant sites, but in tumours likely to be resistant considerable palliative relief may be provided by such a procedure.

The relation between simple goitre and carcinoma of the thyroid is proved by the high incidence of malignant disease of the thyroid in endemic centres and by the frequent history of a pre-existing goitre. The probability that most cases of carcinoma commencing in a pre-existing goitre begin in a fœtal adenoma is a sound reason for recommending the removal of all solitary adenomata without delay. Adenomata should be removed by enucleation-resection rather than by enucleation alone. The advisability of operation should also be considered in other forms of nodular goitre.

The analysis, while of some value, does not clearly indicate the best method of treatment to be adopted, but in view of the obvious importance of the histological type of the tumour it was decided to carry this aspect of the investigation further.

THE RADIOSENSITIVITY OF THE DIFFERENT HISTOLOGICAL TYPES

In determining the radiosensitivity of the three histological subdivisions account was taken, in this analysis, only of the rate of response of the tumour tissue treated irrespective of whether the primary tumour itself or only a gland or metastatic deposit was being treated. If the tumour diminished rapidly in size it was regarded as radiosensitive and all other cases were placed in the radioresistant category. The survival rate was ignored because clearly a case might respond well in the treated area and yet die in a short time from some other known or unknown deposit.

In 19 cases where the X-ray treatment followed surgery it appeared possible that all the tumour tissue had been removed and these cases were, of course, excluded from the analysis. In a further 61 cases either no X-ray treatment was given or else the dosage was so low that no useful assessment could be made. In the remaining 64 cases sufficient dosage was given to the clinically obvious tumour to determine its sensitivity. The results are shown in Table X.

TABLE X

RADIOSENSITIVITY

Radiosensitivity Determined	64
? No Tissue to test Radiosensitivity	19
No treatment or palliative treatment	61
Total ..	144

	Adeno-carcinoma	Pap.adeno-carcinoma	Undiff. carcinoma	Type unknown	Total
Radiosensitive	0	0	11	17	28
Not radiosensitive	7	3	9	17	36
Total	7	3	20	34	64
%Radiosensitive	0%	0%	55%	50%	44%

Somewhat surprisingly it was found that all the tumours proving to be radiosensitive were in the completely undifferentiated category. The numbers of differentiated tumours are too small for the conclusion to be drawn that all differentiated tumours are radioresistant and clearly further observations require to be made.

The other interesting point is that all the undifferentiated tumours were not radiosensitive—in fact only 55% were radiosensitive. So far it has not been possible to distinguish these two types from one another by histological examination, thus recalling an observation made in a previous communication to this Society where it was shown that the radiosensitive and the radioresistant meningiomata cannot be distinguished from one another by means of histological examination. (*Proc. R. Soc. Med.*, 1946, 39, 673.)

However, other findings are of some help in distinguishing the radiosensitive group. The average duration of symptoms in the radiosensitive cases was 6·3 months and of the radioresistant cases sixteen months. Of the 28 radiosensitive cases only three had pre-existing adenomata and the tumour as a rule involved the gland diffusely, producing a smooth uniform enlargement of the whole gland.

It will be noted that of the 64 cases 44% were radiosensitive and therefore suitable for treatment by radiotherapy. The five year survival rate however is poor in these cases because of the early spread of cells to distant sites. Where death took place in a short period of time it was found that most of the patients died from metastases

Section of Neurology

President—DOUGLAS MCALPINE, M.D.

JOINT MEETING WITH THE SOCIÉTÉ DE NEUROLOGIE DE PARIS HELD ON APRIL 15 AND 17, 1947

[*April* 15, 1947]

DISCUSSION ON PENICILLIN IN NEUROLOGY

Sir Hugh Cairns: *Penicillin in suppurative conditions of the brain and meninges* [Abstract].—This paper summarizes four years' experience in the use of penicillin in pyogenic infections of the brain and meninges.

THEORY OF PENICILLIN TREATMENT

(1) *General theory.*—Penicillin must be given access to all infecting organisms; the limited powers of penicillin to penetrate any large non-vascular area of infection have not always been fully appreciated. The application of this principle in treatment of brain wounds, brain abscess, and pyogenic meningitis was discussed.

(2) *Intrathecal penicillin.*—Dosage and routes were discussed. Increasing the dose does not increase the persistence of penicillin in the C.S.F. or the survival rate in meningitis, and it may do harm.

(3) *Subdural penicillin* passes rapidly into the blood-stream. Consequently, for purulent pachymeningitis, subdural injections should be given every four to six hours. Exceptionally penicillin disappears rapidly from the subarachnoid space by leakage into the subdural space.

(4) *Systemic penicillin* does not pass into the C.S.F. in adequate amounts, but is of subsidiary value in most intracranial infections for a variety of reasons.

Results of treatment.—The immediate treatment of a bacteriologically unidentified meningitis should be by systemic sulphonamides and systemic penicillin. Intrathecal penicillin should usually not be given until the organism in the C.S.F. has been identified and aseptic precautions can be exercised in its use; but in fulminating meningitis it may occasionally be necessary to use penicillin intrathecally immediately.

Leptomeningitis will be discussed by my colleague Dr. Honor Smith.

Purulent pachymeningitis.—This condition is most commonly produced by a non-B. hæmolytic streptococcus, spreading from osteomyelitis of the skull secondary to infection of the paranasal sinuses. Pus spreads in the subdural space, paralysing the underlying brain cortex. Formerly this condition was almost invariably fatal but since penicillin has been freely available, we have saved 6 of 11 patients.

Brain abscess.—With the help of penicillin it has been possible to extirpate successfully cerebellar abscess and, following the work of Le Beau, bronchogenic abscess. Thus, complete extirpation of brain abscess, which we owe to the classic work of Clovis Vincent, has now become the standard method of treatment for almost all varieties of brain abscess. Though penicillin has greatly improved the prospects in the more difficult types of brain abscess, it has in no way diminished the need for unremitting expert care in each individual case.

Prevention of infection of operative wounds.—For over two years a powder of calcium penicillin mixed with sulpha-mezathine (5,000 units per gramme) has been insufflated into all clean operation wounds. This gives a level of over 0·02 u./c.c. penicillin in the wound juices for twelve to eighteen hours, sufficient to inhibit the growth of the common pyogenic contaminants of the wound during that period. With this powder the incidence of post-operative infection, as compared with its incidence in the previous six and a half years, has been significantly reduced.

Dr. Honor V. Smith (*Nuffield Department of Surgery, Oxford*): *The treatment of leptomeningitis with penicillin.*—Most of our work on the treatment of meningitis with penicillin has been done on pneumococcal meningitis (Smith, Duthie and Cairns, 1946), but we have found

METHOD OF X-RAY TREATMENT

Until recently the method of X-ray treatment used consisted of two opposed lateral fields to the thyroid gland and treatment was regarded as complete if a minimum dose of 3,500 r was delivered to the tumour in three weeks or less. A single anterior field was used to treat retrosternal carcinomata and to treat retrosternal extensions of a carcinoma in the neck.

When the local response to X-ray treatment was good local recurrences did not take place subsequently but the results were poor on account of the high tendency of these tumours to metastasize to the lungs. In an attempt to overcome this difficulty, and because the tumours worth treating by radiotherapy are generally highly radiosensitive, it was decided to treat all undifferentiated tumours by wide-field X-ray therapy. The field extends from the chin above to the lower limits of the thorax below. Anterior and posterior fields are used and a surface dose of 2,500 r is given in daily fractions over approximately five weeks. If during the course of treatment it is seen that the primary tumour is not responding the wide-field treatment is stopped and the patient is given localized treatment to the thyroid gland only. It is hoped by including the thorax it will be possible to raise the survival rate of the radiosensitive tumours and the immediate results can be regarded as promising.

Care must be taken in all cases treated by wide-field X-ray treatment to avoid producing at a later date a serious or even fatal anæmia. Observations in thyroid and in other tumours indicate that this difficulty can be overcome by carefully noting the blood platelet level and by terminating treatment if the platelet count should fall below 100,000 cells per c.mm. Further details of this work will shortly be published by Dr. W. Court Brown to whom we are indebted for the examinations made.

CONCLUSIONS

While the direct comparison of treatment methods proved impossible the other observations indicate reasonably clearly that the following points can meanwhile be accepted as a useful working basis until they are modified by further observations.

(1) If the patient has a localized nodule of some standing and the case is operable (as defined) every effort should be made to remove the tumour radically by surgery. The value of subsequent X-ray therapy is doubtful if the tumour proves to be an adenocarcinoma or a papillary adenocarcinoma, but as the observations were made on a limited number of cases it would be wise to continue its use until a more definite statement can be made. If the case proves to be an undifferentiated carcinoma post-operative X-ray treatment should be given.

(2) If the patient has diffuse uniform enlargement of the whole or greater part of the thyroid gland and if the duration of the swelling is short the tumour is probably an undifferentiated carcinoma and X-ray treatment is indicated. If present methods prove successful wide-field X-ray treatment should be given so as to include the thorax.

(3) A biopsy should be obtained in all cases where this is possible so that further evidence may be obtained regarding the value of the histological type of the tumour as a guide to the best method of treatment. If, however, dyspnœa is very marked X-ray treatment should be commenced immediately because any delay in these cases may lead to the death of the patient.

(4) Surgical removal of as much tumour tissue as possible in an advanced carcinoma which clinically is possibly an undifferentiated carcinoma should not be attempted because the surgical interference must increase the risk of dissemination of tumour cells outwith the area to be irradiated.

cranial abscess is present it is imperative to give the intrathecal penicillin by ventricular injections as in such cases lumbar and cisternal injections are not only useless but highly dangerous. Further, the abscess itself demands surgical treatment on the lines already described by Sir Hugh Cairns (1947).

Meningococcal meningitis.—Intrathecal penicillin is rarely required in the treatment of meningococcal meningitis since the results obtained by sulphonamides alone are excellent. It is, however, indicated if the patient shows signs of sulphonamide intolerance or when he is vomiting persistently or is so severely dehydrated that sulphonamide therapy carries a grave risk of renal block. It is also indicated in the rare cases when the response to sulphonamides is disappointing.

CONCLUSION

Finally, the penicillin therapy of meningitis must be supplemented by the closest observation of the patient and the best of nursing care. No two cases are ever quite alike and each must be treated on its own merits. If these conditions are fulfilled recovery should be expected. Comparison of the results obtained in our first 38 cases with those of a series of cases treated in the same hospital on sulphonamides alone, illustrates the change in prognosis brought about by the introduction of penicillin (Smith, Duthie and Cairns, 1946, fig. 8).

REFERENCES

CAIRNS, H. (1947) *Brain* (In press).
KINSMAN, J. M., and D'ALONZO, C. A. (1946) *New Engl. J. Med.*, 234, 459.
SMITH, H. V., DUTHIE, E. S., and CAIRNS, H. (1946) *Lancet* (i), 185.
——, SCHILLER, F., and CAIRNS, H. (1946) *Proc. Roy. Soc. Med.*, 39, 613.

Dr. C. Worster-Drought: *Penicillin in neurosyphilis* [Abstract[1]].—Penicillin has a definite and established place in the treatment of neurosyphilis.

Most of the present-day experiences of penicillin treatment in neurosyphilis are based on the "standard" course established in 1944 for the treatment of early syphilis in the British Services and in the U.S. Army in Europe, viz.: a total dosage of 2,400,000 international units given by parenteral injection every three hours, day and night, for seven and a half days.

In view of the percentage of relapses even in early syphilis (7-15%) it is doubtful if this course is sufficient for neurosyphilis. It is suggested that a total dosage of at least 3,000,000 units be given to all cases of neurosyphilis and that in parenchymatous neurosyphilis the total dosage should reach 4,000,000 to 5,000,000 units.

It may eventually prove unnecessary to keep penicillin in the blood at as high a continuous level as possible throughout the period of treatment. If so, equally good therapeutic effects might be obtainable with larger doses of penicillin given at longer intervals (300,000 units given every twelve hours or 500,000 units every twenty-four hours for eight to fifteen days). Such a method would enable cases of chronic neurosyphilis to be treated as out-patients.

Intramuscular injection is the best method of administering penicillin. For various reasons, the intravenous route—either by continuous drip or by repeated single injection—has little to commend it.

If it is eventually shown that a continuous and fairly constant level of penicillin in the blood is really necessary for full therapeutic effects, the preparations of penicillin in oil and beeswax may prove useful. It has been shown that following a deep subcutaneous injection of 300,000 units in oil-wax, penicillin can be found in the blood serum for sixteen to twenty hours but not at the end of twenty-four hours. Thus, cases of neurosyphilis could be treated as out-patients with one injection of 300,000 units daily for ten to fourteen days. A disadvantage is that persistence of the oily preparation in the tissues has been reported and that occasionally a localized and tender induration appears three days after injection of the oil-wax penicillin. Further trials are necessary.

There is no evidence that the intrathecal administration of penicillin is of greater therapeutic value in neurosyphilis than when the remedy is given by intramuscular injection. Owing to the resulting reactions and the various additional risks, intrathecal injection of penicillin is best avoided in most cases of neurosyphilis.

Owing to the risk of possible Herxheimer-Jarisch reactions following the first doses of penicillin, all cases of neurosyphilis should receive an initial series of bismuth injections before starting the full course of penicillin.

In view of the percentage of relapses reported in cases even of early syphilis treated with penicillin alone and in spite of the initial beneficial effects following penicillin treatment, the author has at no time abandoned the use of arsenicals and bismuth—used in conjunction our methods applicable to any variety of meningitis in which the infecting organism is sensitive to penicillin. These methods will therefore be briefly described together with the principal difficulties we have encountered.

---

[1] Published in full: *Brit. med. J.*, 1947 (ii), 559.

Our routine treatment in an uncomplicated case is as follows (Smith, Duthie and Cairns, 1946, fig. 1): penicillin is given once or twice daily for a minimum of five days by intrathecal injection in doses of 8,000 to 16,000 units, made up in solutions of 2,000 units per c.c. We have found that larger doses than this, especially when given in concentrated solution, are no more effective and may actually be harmful. Intrathecal injections are essential because penicillin will not pass from the blood to the C.S.F. in anything except minute amounts (Kinsman and d'Alonzo, 1946; Smith, Duthie and Cairns, 1946). Intrathecal penicillin may be given by the lumbar, cisternal or ventricular injection; occasionally it is necessary to use all three routes, but in uncomplicated cases we have found the lumbar route safe, convenient and effective. In addition to intrathecal penicillin, sulphonamides are given in full doses and up to the present time we have found sulphadiazine the preparation of choice. This is given to supplement the intrathecal penicillin. The latter can only be fully effective when it can circulate freely in the C.S.F. and thus reach all parts of the cerebrospinal pathways. To achieve this, it is essential that these pathways are patent and we have evidence that sulphonamides are able to prevent or delay the deposition of fibrino-pus which, in the untreated case, is so apt to block these pathways. Sulphonamides should be given as soon as meningitis is diagnosed as they will often tide the patient over the interval which may elapse before treatment with penicillin can be begun. They are also useful for covering the period in which intrathecal penicillin is withheld.

Penicillin is also given systemically in the usual doses because in the majority of cases pneumococcal meningitis is secondary to an overt primary focus of infection (Smith, Duthie and Cairns, 1946, fig. 2). While we do not depend on the systemic penicillin to influence the course of the meningitis itself, we have found it valuable in controlling the primary focus of infection. For example, in otogenic meningitis, the commonest variety of both pneumococcal and streptococcal meningitis, we consider that operation on the ear is no longer indicated during the acute stage of the illness (Smith, Schiller and Cairns, 1946). Further, pneumococcal meningitis may either be caused, or complicated by septicæmia and for this also systemic penicillin is invaluable.

COMPLICATIONS

Spinal block.—Unfortunately complications are common and the two that we have met with most frequently are spinal block and relapse of the meningitis. Spinal block is seen in the acute stage of the illness, when it is presumably caused by the deposition of fibrino-pus, and may also develop after some days when chemotherapy has been delayed or inadequate. We have also seen it following lumbar injections of 50,000 units or more of penicillin, especially when concentrated solutions have been used. The first sign of impending block is difficulty in obtaining fluid at lumbar puncture. Whenever this occurs penicillin should be given by cisternal or, preferably, by ventricular injection, as lumbar injections are rendered useless.

Relapse.—Relapses are also common; 16 of our 50 patients relapsed one or more times before finally recovering. In one case the patient relapsed eight times and in each relapse was as ill as in the original attack of meningitis (Smith, Duthie and Cairns, 1946, fig. 3). The treatment of relapse does not differ from that of the initial attack and the prognosis is good provided that each relapse is promptly recognized and energetically treated.

RESULTS

We have now treated 50 unselected cases of pneumococcal meningitis with 39 recoveries. In 11 fatal cases, 2 patients died of causes other than meningitis; of the remaining 9, 4 patients were virtually moribund when admitted to hospital and died within a few hours of receiving their first injection of penicillin. Delay in the institution of treatment was thus the commonest cause of failure in our series and was most often due to delay in diagnosis. In the fulminating case, pneumococcal meningitis develops with extreme rapidity and the differential diagnosis is from subarachnoid hæmorrhage. Such cases are among the most acute of all medical emergencies and a few hours delay in instituting penicillin therapy may make the difference between death and complete recovery.

Streptococcal meningitis.—Penicillin therapy carried out on the lines just described is indicated also in streptococcal and staphylococcal meningitis. In our experience, which is admittedly limited, we have found that streptococcal meningitis is relatively frequently complicated by intracranial abscess (Smith, Schiller and Cairns, 1946, fig. 2). If an intramalaria. It is hoped that in future these different methods of treatment will be more evenly balanced and that one will be in a position to evaluate the relative merits of such courses, if any such distinction can be discovered. Penicillin has been administered intramuscularly in every case—the dosage employed has been 300,000 units daily in one injection for fourteen days, giving a total of 4·2 mega units. The penicillin used has been sodium penicillin dissolved in sterile distilled water.

In the first place patients given penicillin only were carefully selected. They were all of poor physical condition, their malaria risks were high and in many of them the prognosis was regarded as relatively hopeless. This probably explains why 6 out of 14 cases have died. The remaining 51 cases treated by different combinations of malaria and penicillin are still alive. Of the 6 cases who died, 2 died of intercurrent disease, coronary thrombosis and acute purulent bronchopneumonia ; a third died of aortic disease; the remaining three died of G.P.I. Two cases were very advanced and the third case can be described as a fulminating type.

While it is not possible to give any percentages, owing to the small number of cases under review, we have been impressed by certain features of the clinical results. One of the most striking was the improvement noticed in many patients during the actual course of penicillin, which is a phenomenon rarely, if ever, seen during malaria therapy. This improvement was both physical and mental in character. Patients showing improvement with penicillin who were unfit for malaria on admission became well enough to receive a course of fever, though a certain proportion of them were only fit for a modified course, e.g. 3-5 peaks of 103° F. or over. The most dramatic results were seen in patients who were confused and in poor physical condition. Penicillin was administered to 8 patients with cardiovascular lesions, 4 with cardiovascular degeneration, 2 with aortic regurgitation and 2 with syphilitic aortitis. No Herxheimer reactions were encountered and no preparatory course of a heavy metal and potassium iodide was given.

Case 1189.—Male, aged 40. Admitted 12.12.45. Grandiose, elated, very excited and violent; physically emaciated and in very poor general condition. History of mental symptoms for about eight weeks.

Physical signs—A.R. pupils. Tremors of tongue and fingers. C.S.F.: W.R. $+30^{+}$, Cells 5 per c.mm., Protein 80 mg.%, Lange 5555432100.

In view of his very poor physical condition he was considered unfit for malaria and so was given penicillin 300,000 units intramuscularly for fourteen days. His condition deteriorated steadily, both mentally and physically, and this fulminating case of G.P.I. died 26.2.46, six months from the date of onset of symptoms.

Case 1249 (Maudsley Hospital).—Male, age 46. Admitted 21.5.46. This patient's symptoms dated from August 1944, following a bad flying-bomb raid. After exhibiting emotional instability for several months, he developed a confusional attack and in December 1945 got lost in a street. His mental condition considerably deteriorated and it was not until May 1946 that he was admitted into hospital. His physical condition then revealed ocular signs—unequal pupils, left A.R.; speech slurred; poor co-ordination with an unsteady gait and a positive Romberg. He received treatment by penicillin 300,000 units daily for fourteen days, to a total of 4·2 mega units. During the course of penicillin his speech became more distinct, his replies to simple questions were less rambling and his physical condition improved. He continued to improve and was discharged home on 20.7.46.

Six months later he attended the follow-up clinic. He appeared simple and childish, but was at work doing internal house repairs. His clinical condition was paralleled by a serological one.

Before treatment—Blood: W.R. $+30^{+}$, Kahn ++++. C.S.F.: W.R. $+30^{+}$, Cells 15 per c.mm., Protein 50 mg.%, Lange 5555432100.

Six months after treatment. Blood: W.R. +10, Kahn ++++. C.S.F.: W.R. +6, Cells 3 per c.mm., Protein 90 mg.%. Lange 5554321000.

We are satisfied that penicillin will prove a useful adjunct to malaria; whether penicillin will supersede malaria is doubtful; only the lapse of time will enable us to come to definite conclusions. We know that malaria alone for the established case of G.P.I. should be supplemented by some additional form of therapy. It may well be that penicillin will prove the optimum choice. Moreover, the combination of penicillin and malaria may make possible the reduction of the number of peaks of fever generally aimed at. The optimum dosage of penicillin and the length of treatment have yet to be settled, and it is only by trial and error and the continued follow-up of cases treated by different regimens that we can arrive at the proper answer.

To summarize our clinical observations:

The majority of patients who improved began to do so during the actual course of penicillin.

Patients showing improvement with penicillin, who were unfit for malaria on admission, became well enough to receive a course of fever, though a certain proportion of them were only fit for a modified course, i.e. 3-5 peaks of 103° F. or over.

The most striking clinical results were seen in patients who were confused and in poor physical condition.

with penicillin—in the treatment of neurosyphilis. It is even possible that a "synergistic" action exists between the two types of treatment as indicated by the animal experiments of Eagle and his co-workers and the observations of Levaditi and Vaisman (1946).

Three injections of arsenical and bismuth can be given during the week of penicillin treatment and then follow 12 injections each of arsenical (neoarsphenamine, mapharsen or acetylarsan) and bismuth at weekly intervals. It is necessary to repeat the courses of arsenical and bismuth according to the type of case.

Penicillin in adequate dosage and administered by whatever route has a striking initial beneficial effect on all forms of meningovascular neurosyphilis and especially acute forms. The pleocytosis and the increased protein of the cerebrospinal fluid will often show a noteworthy decrease within a few days of starting treatment and will frequently reach a normal level within two to four weeks. The intensity of the Wassermann reaction in the cerebrospinal fluid gradually decreases and may become negative within two to four months. There is no parallel action on the blood Wassermann reaction which may continue positive for many months and even indefinitely in cases limited to penicillin treatment.

General paresis is best treated with an initial course of penicillin of total dosage 4,000,000 to 5,000,000 units followed by full malarial or fever therapy (10 to 12 malarial rigors). Finally, the usual courses of arsenical and bismuth are advisable until the serological reactions become negative.

In cases of general paresis (and taboparesis) in which malarial or fever therapy is contra-indicated by reason of cardiovascular disease, one must rely on penicillin alone. Some improvement—but not cure—can be expected.

In tabes dorsalis no dramatic change follows penicillin treatment. Cases are best treated with an initial course of penicillin and then with the usual courses of arsenical and bismuth for two to four years, until apparently quiescent and the serological reactions have become negative.

Special symptoms such as "lightning pains" and "gastric crises" benefit from penicillin in some cases, including those in which the serological reactions are already negative.

Primary optic atrophy of syphilitic origin can be arrested in a fair proportion of cases by malarial therapy. Penicillin alone is not likely to arrest the optic atrophy but may prove useful in hastening arrest or in bringing about arrest in an even larger proportion of cases. Treatment should consist of an initial course of penicillin of total dosage 4,000,000 units to 5,000,000 units, followed by full malarial therapy (10 to 12 rigors) and afterwards arsenical and bismuth. Observation of any case of syphilitic optic atrophy must extend to five years or longer before any form of treatment can claim success.

A distinction must be drawn between "Early asymptomatic neurosyphilis" and "Late asymptomatic neurosyphilis". The latter condition, being of serious import, must be treated with penicillin and malarial or fever therapy on the same lines as "general paresis".

It will not be possible fully to assess the final results of penicillin treatment in neurosyphilis—even when combined with the older methods—for several years. The necessity for the careful and prolonged "follow up" of cases is imperative. We can only wait and ascertain what proportion of the thousands of cases of early syphilis treated with penicillin alone in the British and United States Forces will eventually relapse or develop some form of neurosyphilis. Consequently, as a result of further observations, it may be necessary to amplify, extend, or otherwise alter the schemes of treatment advocated.

REFERENCES

EAGLE, H., MAGNUSON, H. J., and FLEISCHMAN, R. (1946) *Ven. Dis. Informat.*, 27, 3.
LEVADITI, C., VAISMAN, A. (1946) *Bull. Acad. Méd. Paris*, 130, 30.

Dr. W. D. Nicol and Dr. M. Whelen (*Malaria Therapy Centre, Horton Emergency Hospital*): *Penicillin and neurosyphilis.*—In this very brief communication we would at once stress the fact that at this time our knowledge of the use of penicillin in the treatment of G.P.I. and neurosyphilis is both inadequate and incomplete. Moreover, the number of cases treated is small, 57, all of whom, with the exception of 2 cases treated at the Maudsley Hospital, were admissions to the Malaria Therapy Centre at Horton. The majority of cases, 42, were general paretics; in addition there were 6 tabetics, 4 taboparetics, 2 congenital neurosyphilitics, 1 cerebral syphilitic, 1 psychopath with neurosyphilis and 1 late asymptomatic neurosyphilitic. To assess the value of any therapeutic measures one should examine the clinical condition and the cerebrospinal fluid at regular intervals. We are not in a position to assess serological results owing to the short time that has elapsed since treatment, and are, therefore, compelled to confine our observations to clinical results.

Of 57 cases treated, 14 were given penicillin only, 7 received a subsequent course of malaria, 6 received penicillin and malaria concurrently and 30 were given a course of penicillin after with the classical symptoms that reveal disturbance of functions of the heart, the kidney or the brain.

(2) *The permanent form* of cerebral œdema due to arterial hypertension is perhaps the more frequent; the clinical picture is one of intracranial pressure, which resembles that seen in a case of brain tumour: headache more or less permanent, vomiting, slow cerebration and drowsiness. Transient loss of sight or progressive diminution of vision is an early important feature, caused by neuroretinitis of the fundi with hæmorrhages and with spots, especially in the macular region. But this is an advanced state of the lesion. At the beginning the fundus may present the appearance of a choked disc and the question of a tumour of the brain may arise, the high blood-pressure, the increase of arterial retinal pressure, the signs of retinal arteriosclerosis with associated cardiac or nephritic symptoms will be important arguments in favour of the diagnosis of cerebral œdema with neuro-retinitis; but, in certain cases, the diagnosis may be difficult, especially at the early stage of the affection, since a tumour of the brain may occur in a patient with high arterial pressure.

The evolution in this form is often variable; there can be improvement occurring spontaneously or as a result of therapy. The condition tends to be progressive and the prognosis is serious, the cerebral œdema progressing invariably, and to the blindness caused by the retinal œdema, are added intense headache, progressive drowsiness and death in some months in a state of cachexia, if it is not accelerated by other vascular cerebral complications or by nephrocardiac deficiency.

The *diagnosis* of the *acute form* of meningo-cerebral œdema is, as a rule, easy, the other vascular accidents due to arterial hypertension (cerebral hæmorrhage and softening of the brain) having a different symptomatology and evolution. The only difficulty in diagnosis would be with a subarachnoid hæmorrhage. Lumbar puncture makes easy the recognition of the latter condition by the appearance of the fluid; however, one can see the association of both syndromes.

In the case of the *permanent form* of cerebral œdema, the question of a tumour of the brain, in a patient having a permanent high arterial pressure, may arise. Ventriculography may be necessary, but it must be realized that dilatation of the ventricles can exist in the brain of patients with cerebral œdema and this finding must not be taken as a sign of tumour or circumscribed meningitis of the posterior fossa.

Pathological study of meningo-cerebral œdema must be done on the fresh brain. After opening the dura, one sees the pericerebral subarachnoidal space filled with an increased quantity of fluid; the brain itself is swollen by œdema, especially in the occipital lobes, and is the seat of intense vascular congestion, the smallest branches of the pial nest being visible.

Histological study (made after slow and progressive inclusion by celloidin, which must avoid artificial retractions) shows infiltration of the brain tissue by œdema, with distension of the perivascular and even pericellular spaces, areolar aspect of the cerebral tissue, especially around the vessels, distension and swelling of oligodendroglia, and even reactional cellular alterations. The maximal alterations are in the pia mater, the grey matter of the paraventricular regions and the hypothalamus. Hæmorrhages can be only microscopic in the perivascular spaces, but there may be more important hæmorrhages, especially in basal ganglia and their arterial origin can be demonstrated.

The lesions of the retina in the permanent form are identical: mechanical distension of the tissue by œdema and in places enormous bubbles of œdema corresponding with the white spots seen by ophthalmoscopy; retinal hæmorrhages whose arterial origin can be demonstrated, and lesions of the walls of the small arteries of the retina.

These clinical and pathological data are related to different *pathogenic* problems.

The increase in the local circulation in the brain and retina is obvious; it has an effect, in the permanent form, on the anatomical state of the walls of the vessels, especially on the smallest vessels, consequently the physiology of these vessels must be altered.

It is these structural changes which make possible hæmorrhages whose arterial origin is pathologically demonstrated. But it seems possible, before such anatomical alteration, that water and plasma proteins can pass through the arterial walls in certain conditions.

The increase in local circulation may be the result of an active vasodilatation which opens the bed of many capillaries to the blood flow, or it can be the result of increase of pressure of the cerebral or retinal circulation due to sudden increase of general arterial pressure. Hypertonic hormones have different actions on the cerebral and retinal vessels and on vessels of the general circulation, so that it is the cerebral vessels which will be dilated concurrently with vasoconstriction in the general circulation. Clinical and pathological data are in favour of this interpretation. There is also a place for discussion about the direct mechanism of œdema, first, the conditions influencing the permeability of the small vessels and secondly the reactions of the brain centres to circulatory changes.

Penicillin was administered to 8 patients with cardiac lesions, 4 with cardiovascular degeneration, 2 with aortic regurgitation and 2 with syphilitic aortitis. No Herxheimer reactions were encountered and no preparatory course of a heavy metal and potassium iodide was given.

Penicillin failed to save the lives of one general paralytic of a fulminating type and two very advanced cases, so in this respect it is apparently no more successful than older forms of treatment.

[*April* 17, 1947]

DISCUSSION ON CEREBRAL ŒDEMA

Professor Th. Alajouanine: *Meningo-cerebral œdema caused by arterial hypertension.*—Cerebral œdema must be defined as a special mode of vascular disturbance of the brain. This form of pathological alteration together with other cerebral vascular conditions ranks next to hæmorrhage and softening of the brain, as we have already emphasized in our report on "Morbid Cerebral Circulation" read (with Thurel) at the Annual International Neurological Meeting in Paris in 1936.

By "cerebral œdema" we do not mean the simple œdematous reaction encountered in the neighbourhood of focal vascular lesions of the brain (hæmorrhage or softening); we have in view a generalized and diffuse œdema of the brain and the meninges, directly produced by arterial hypertension and related to a mechanism quite different from that which produces softening of the brain, and cerebral hæmorrhage.

This vascular process can be observed (and in fact has been observed) in various cases of arterial hypertension resulting from different ætiological factors. But the most characteristic and perhaps the most frequent causes of cerebral œdema are: malignant hypertension of young adults and paroxysmal hypertension due to neuro-endocrine disturbances. It may, however, be seen in all forms of arterial hypertension.

The clinical manifestations of meningo-cerebral œdema due to arterial hypertension will be described under two principal headings: (1) In the first group of cases, there are paroxysmal clinical events co-existing with paroxysmal increase of blood-pressure, giving a transient symptomatology that recalls in certain points the clinical picture of a subarachnoid hæmorrhage. The vascular origin of such accidents cannot be mistaken; it is the *acute form* of meningo-cerebral hypertensive œdema;

(2) In a second group of cases, we deal with a permanent morbid state. The clinical picture resembles that of a brain tumour, so prominent are the headache, the drowsiness and the visual disturbances due to a neuro-retinitis (choked disc with retinal œdema). This sort of case constitutes the *permanent form* of cerebral hypertensive œdema.

(1) *The acute form* is not the most frequent, but has the most typical features, though the intensity of the manifestations may vary.

The patient suffers suddenly from an intense headache often with a pulsatile character. Vomiting soon occurs followed by visual disturbances (mist over the eyes or complete loss of sight). Quickly there develops a progressive mental dulling which makes the patient fall into a torpid state, though true coma is rare.

Different kinds of accidents can happen during this stage; periods of restlessness with mental confusion, epileptiform seizures, sometimes of Jacksonian type, sometimes generalized; objective signs of a localized lesion of the brain (monoplegia, hemiplegia and aphasia) ordinarily of short duration. (Pathological observations show that they are due to small arterial hæmorrhages in the basal ganglia.)

Ophthalmoscopic examination may show a hyperæmia of the fundi, exceptionally a choked disc or a small retinal hæmorrhage. Arterial retinal pressure is usually higher than the diastolic arterial pressure.

These various manifestations appearing suddenly, in association with a paroxysm of arterial hypertension, leave no doubt as to the nature of the symptoms.

Lumbar puncture shows an increase of pressure of the cerebrospinal fluid, with oscillations synchronous with the pulse. The examination of the fluid reveals an increase of protein up to 0·01 gramme % with an absence of cellular reaction (albumin-cytologic dissociation).

This form of meningo-cerebral œdema often resolves spontaneously, or after lumbar puncture. The increase of arterial pressure is transient so that in a few days symptoms have disappeared. Headache clears up first, then the mental state improves, finally the sight returns completely or incompletely leaving a permanent hemianopia, sometimes with alexia due to occipital œdema. Ordinarily no permanent sign of paresis remains, at least after the first attack: the latter may reappear with a new paroxysmal rise in arterial hypertension.

The same patient can subsequently have other vascular manifestations, subarachnoid hæmorrhage, cerebral hæmorrhage, or the arterial hypertension may become permanent with the classical symptoms that reveal disturbance of functions of the heart, the kidney or the brain.

(2) *The permanent form* of cerebral œdema due to arterial hypertension is perhaps the more frequent; the clinical picture is one of intracranial pressure, which resembles that seen in a case of brain tumour: headache more or less permanent, vomiting, slow cerebration and drowsiness. Transient loss of sight or progressive diminution of vision is an early important feature, caused by neuroretinitis of the fundi with hæmorrhages and with spots, especially in the macular region. But this is an advanced state of the lesion. At the beginning the fundus may present the appearance of a choked disc and the question of a tumour of the brain may arise, the high blood-pressure, the increase of arterial retinal pressure, the signs of retinal arteriosclerosis with associated cardiac or nephritic symptoms will be important arguments in favour of the diagnosis of cerebral œdema with neuro-retinitis; but, in certain cases, the diagnosis may be difficult, especially at the early stage of the affection, since a tumour of the brain may occur in a patient with high arterial pressure.

The evolution in this form is often variable; there can be improvement occurring spontaneously or as a result of therapy. The condition tends to be progressive and the prognosis is serious, the cerebral œdema progressing invariably, and to the blindness caused by the retinal œdema, are added intense headache, progressive drowsiness and death in some months in a state of cachexia, if it is not accelerated by other vascular cerebral complications or by nephrocardiac deficiency.

The *diagnosis* of the *acute form* of meningo-cerebral œdema is, as a rule, easy, the other vascular accidents due to arterial hypertension (cerebral hæmorrhage and softening of the brain) having a different symptomatology and evolution. The only difficulty in diagnosis would be with a subarachnoid hæmorrhage. Lumbar puncture makes easy the recognition of the latter condition by the appearance of the fluid; however, one can see the association of both syndromes.

In the case of the *permanent form* of cerebral œdema, the question of a tumour of the brain, in a patient having a permanent high arterial pressure, may arise. Ventriculography may be necessary, but it must be realized that dilatation of the ventricles can exist in the brain of patients with cerebral œdema and this finding must not be taken as a sign of tumour or circumscribed meningitis of the posterior fossa.

Pathological study of meningo-cerebral œdema must be done on the fresh brain. After opening the dura, one sees the pericerebral subarachnoidal space filled with an increased quantity of fluid; the brain itself is swollen by œdema, especially in the occipital lobes, and is the seat of intense vascular congestion, the smallest branches of the pial nest being visible.

Histological study (made after slow and progressive inclusion by celloidin, which must avoid artificial retractions) shows infiltration of the brain tissue by œdema, with distension of the perivascular and even pericellular spaces, areolar aspect of the cerebral tissue, especially around the vessels, distension and swelling of oligodendroglia, and even reactional cellular alterations. The maximal alterations are in the pia mater, the grey matter of the paraventricular regions and the hypothalamus. Hæmorrhages can be only microscopic in the perivascular spaces, but there may be more important hæmorrhages, especially in basal ganglia and their arterial origin can be demonstrated.

The lesions of the retina in the permanent form are identical: mechanical distension of the tissue by œdema and in places enormous bubbles of œdema corresponding with the white spots seen by ophthalmoscopy; retinal hæmorrhages whose arterial origin can be demonstrated, and lesions of the walls of the small arteries of the retina.

These clinical and pathological data are related to different *pathogenic* problems.

The increase in the local circulation in the brain and retina is obvious; it has an effect, in the permanent form, on the anatomical state of the walls of the vessels, especially on the smallest vessels, consequently the physiology of these vessels must be altered.

It is these structural changes which make possible hæmorrhages whose arterial origin is pathologically demonstrated. But it seems possible, before such anatomical alteration, that water and plasma proteins can pass through the arterial walls in certain conditions.

The increase in local circulation may be the result of an active vasodilatation which opens the bed of many capillaries to the blood flow, or it can be the result of increase of pressure of the cerebral or retinal circulation due to sudden increase of general arterial pressure. Hypertonic hormones have different actions on the cerebral and retinal vessels and on vessels of the general circulation, so that it is the cerebral vessels which will be dilated concurrently with vasoconstriction in the general circulation. Clinical and pathological data are in favour of this interpretation. There is also a place for discussion about the direct mechanism of œdema, first, the conditions influencing the permeability of the small vessels and secondly the reactions of the brain centres to circulatory changes.

The Treatment is different in both forms of meningo-cerebral œdema, and this is the practical interest of this study.

The acute form suggests the opportunity for an active and immediate therapy; one must fight quickly against the increasing of blood-pressure by removal of a large quantity of venous blood and by vasodilators whose action on the peripheral circulation will help to decrease the cerebral blood flow. One must also try to reduce intracranial pressure and its consequences by withdrawal of cerebrospinal fluid. After the acute period, surgical treatment of the arterial hypertension must be considered in order to avoid the return of other accidents.

The prognosis of the permanent form is less favourable, because of the vascular alterations due to permanent hypertension. Treatment by restriction of salt, hypertonic injections or lumbar punctures has very little result. Surgical treatment is usually contra-indicated because of the state of the vessels, of the kidneys, or of the heart. For the neuro-retinitis, subtemporal decompression has often very little effect.

Dr. Douglas McAlpine said that Professor Alajouanine had introduced a subject which had been rather neglected in this country by neurologists because these cases were usually admitted under a general physician except when the clinical picture was mistaken for that of a cerebral tumour. With regard to the first group of cases, namely those showing acute cerebral symptoms, it was also his experience that they occurred mainly in hypertensive patients over the age of 50. In a series of 15 cases which had been under the care of his medical colleagues at the Middlesex Hospital, the average age was 58. It was difficult to fit in the clinical picture seen in this group, namely the abrupt onset of headache, the disturbance of consciousness, the occasional fit and the rapid clearing up of symptoms, with the conception of a generalized cerebral œdema. Furthermore, papillœdema was usually absent in these cases and the C.S.F. pressure was seldom raised. But, as Professor Alajouanine had pointed out, there might be all grades of cerebral œdema varying from a generalized to a local process. However, his own view, based on the work of Volhard (1931), had been that in this form of hypertensive cerebral attack œdema was not such an important factor as anoxia. The precipitating factor was a sudden additional rise in blood-pressure accompanied by a generalized vasoconstriction. Some years ago he had published a case of hypertension in which during the course of four hours the systolic pressure rose from 210 to 300 at which figure a series of epileptiform attacks occurred. Three hours later the blood-pressure had fallen to its previous level and the patient was free from cerebral symptoms (McAlpine, 1933).

In the second group of cases a rapid rise in blood-pressure was also responsible for the cerebral symptoms. In this group there was no doubt about the existence of cerebral œdema since papillœdema and a raised C.S.F. pressure were characteristic features. In a group of 32 cases collected from the records of the Middlesex Hospital, in which, as far as possible, chronic nephritic cases had been excluded mainly by post-mortem examination, the average age at the onset of cerebral symptoms was 42. Headache and visual disturbances were complained of almost constantly by these patients. In only two instances had a fit occurred prior to admission or during the patient's stay in hospital. This finding contrasted with the more frequent occurrence of fits in the older hypertensive patient, and suggested that cerebral œdema *per se* is not an important factor in the production of fits in hypertension. All cases showed papillœdema with or without retinal changes; the diastolic blood-pressure ranging from 180 to 130 on admission. Professor Alajouanine had suggested that in this group of cases when signs of cerebral œdema were established only exceptionally did they clear up; he thought that there would be general agreement on this point since these cases generally followed the well-known course of malignant hypertension. Exceptionally one might come across a case of marked hypertension over the age of 50 with mild papillœdema which later subsided. In addition there were also rare cases in whom all the features of malignant hypertension were present but after some months these cleared up, the patient subsequently enjoying good health for a number of years. He recalled the case of a young woman aged 24 who was under the care of Dr. Bedford in 1931, complaining of severe headache, dimness of vision and loss of weight. She showed 5D of papillœdema with retinal hæmorrhages and exudate. The blood-pressure was 220/150 and C.S.F. pressure was high. The urea clearance test gave her a figure of 36% of normal. After several weeks in hospital she was discharged free from headache and with considerable subsidence of the papillœdema. In 1932 she returned to work having gained 1½ st. in weight. Her blood-pressure became stabilized about 220/140. She remained at work symptom-free until 1942 when she died of a subarachnoid hæmorrhage. A case of equal interest was the following:

J. M., male aged 42, in January 1936 following an attack of influenza, complained of headache, particularly at night. In March he noticed dimness of vision in the right eye, frequency of micturition at night and loss of weight. Between April 14 and 15 he had eight generalized epileptiform attacks. When examined on the 14th by Dr. E. V. Slaughter he showed early papillœdema with retinal hæmorrhages and exudate. Blood-pressure 220/130. Urine: albumin ++. Cerebrospinal fluid pressure 250 mm.; cells and protein normal. Following these attacks he remained in a stuporose condition.

30.4.36: Admitted Neurological Ward, Middlesex Hospital. He appeared conscious but stuporose. Marked neuro-retinitis with reduction of vision. Heart not enlarged; apex beat thrusting; heart sounds normal; pulse small volume. Blood-pressure 210/130. C.S.F. pressure 230 mm. Blood urea 40 mg.%. Despite repeated venesection and hypertonic salines intravenously, his condition worsened and oliguria became marked.

4.5.36: Patient in coma; Cheyne-Stokes respiration. Papillœdema about 3D.

5.5.36: 4 p.m., coma deeper. Pupils inactive. Blood-pressure 190/150. 1 c.c. mercurial diuretic (salyrgan) given.

6.5.36: a.m., semi-comatose. Signs of right-sided hemiplegia. Profuse sweating. Blood-pressure 118/90. Still incontinent. Blood urea 120 mg.%.

7.5.36: Conscious. Partially aphasic. Can move right arm and leg. Blood-pressure 130/90. No longer incontinent. Urinary output 90 oz. in twenty-four hours.

Subsequent progress: A mercurial diuretic was given daily until May 13. The hemiplegia and aphasia quickly cleared up. Blood-pressure rose and became stabilized at about 190/110-120. Papillœdema subsided and retinal changes slowly resolved. The albuminuria ceased, the blood urea fell to normal but the urea clearance test showed 50% diminution in function. 29.6.36: patient was discharged from hospital free from symptoms. He gained nearly 2 st. in weight in the next three months. He returned to work in the autumn of 1936 and has remained at work since then.

In 1939 Dr. E. Bedford reported that his heart was not enlarged. Blood-pressure 190/110.

March 1947: Free from symptoms. No nycturia. Discs both pale; arteries constricted; otherwise fundi normal. Vision: right J4, left J1. Heart not enlarged. Blood-pressure 190/108. E.C.G. normal. Urine: no albumin.

This case presented a picture of malignant hypertension in its early phase. A mercurial diuretic produced widespread vasodilatation with a dramatic fall in blood-pressure. Presumably the vicious circle of vasoconstriction and hypertension was broken before the irreversible changes in the arterial wall, characteristic of the malignant form of hypertension, were reached.

Dr. McAlpine hoped that as a result of Professor Alajouanine's paper neurologists might study afresh some of the cerebral problems presented by arterial hypertension.

REFERENCES

McAlpine, D. (1933) *Quart. J. Med.*, 26, 463.
Volhard, F. (1931) Handbuch der inneren Medizin, Berlin 2nd ed., 6, i.

Doctors Clovis Vincent, Jacques Le Beau et Gerard Guiot (*Hôpital de la Pitié, Paris*) : *Brain œdema in neuro-surgery.*—The present study on brain œdema is divided into four parts.

(1) Subacute and chronic brain œdema associated with tumours of the brain with special reference to two of its complications, i.e. temporal herniation below the tentorium and cerebellar herniation above the tentorium.

(2) Acute brain œdema as seen during operation, experimental surgery and in cases of severe head injury.

(3) The classification of different varieties of brain œdema.

(4) The surgical treatment of brain œdema with particular regard to temporal herniation.

To us brain œdema and brain swelling are considered as one thing from a practical point of view even if they have a different underlying pathology. Neuro-surgeons speak of "cerebral œdema" when they find a brain tending to increase in volume. This cerebral turgescence may occur independently of ventricular dilatation as for example in craniocerebral injuries. It may also occur to a marked degree in association with small new growths and may be seen in an exploratory burrhole when the dura is opened. The volume of the brain increases and the different parts of the brain tend to bulge out through the foramina and dura. In the process the convolutions are broadened and flattened, the sulci tend to be eliminated and the brain matter is often so soft that a ventricular needle sinks in under its own weight. Œdema caused by cerebral tumour is not distributed evenly throughout the whole brain for it is more marked in the cerebral hemisphere and in the areas adjacent to the tumour. As a result of this other parts of the brain are compressed, even at a considerable distance from the point of maximal œdema.

I.—Subacute and Chronic Brain Œdema in Tumours and Cerebral Abscess

(*a*) *Supra-tentorial tumours.*—Cerebral œdema in fact dominates intracranial pathology in neuro-surgery and clinically is responsible for the production of intracranial hypertension (as evidenced by headache, vomiting and choked disc) more than the actual tumour itself, which, in the case of slowly growing lesions, may reach an enormous volume without raising the intracranial pressure [3].

Cerebral œdema may also be responsible for mistakes in diagnosis as symptoms might appear related to parts of the brain which are unaffected directly by the tumour. Death in all cases is due to a lesion of the brain-stem, either from neoplastic invasion, local traumatic injuries of the brain-stem or lesions due to cerebral œdema. Such lesions may be either an œdematous swelling of the brain-stem, altering or suppressing its functions, or direct pressure on the stem by a "temporal pressure cone" (fig. 1). Temporal pressure cone is the major complication of tumours involving the cerebral hemispheres and may develop very insidiously [2], [3], [7]. In the early stages many cerebral tumours are diagnosed clinically either by local symptoms only or by cerebral œdema. It is only after some time has elapsed that new symptoms and signs, due to the temporal herniation, appear in the form of stiffness of the nape of the neck, rotation of the head, dimming of the intellectual faculties, flushing of the face, dry lips, inability to stand, monoplegia or hemiplegia, convulsions or decerebrate fits. Radiographs show thinning of the underlying bone, and in particular, of the sella turcica [4]. Ventriculography, which may be dangerous, often shows a dilatation of one foramen of Munro with deviation of the third ventricle to the side opposite to the tumour. The whole of the third ventricle is deviated when the temporal herniation is complete but is only partially deviated in incomplete herniation; in the latter case only the superior part of the third ventricle is shifted (figs. 2 and 3).

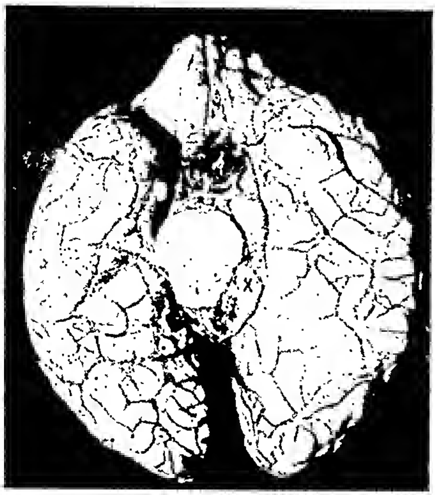


FIG. 1.—Typical temporal herniation (x).

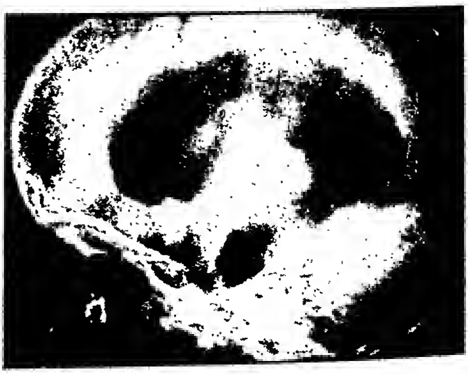
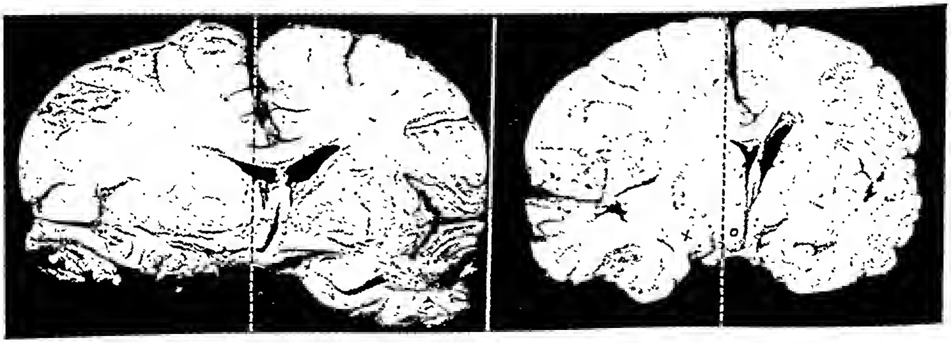


FIG. 5.—Ventriculogram. Gross appearance of tumour of posterior half of third ventricle. Actually it is a shift upward and forward of the third ventricle by upward cerebellar herniation (cerebellar tumour).



A B

FIG. 2.—Third ventricle and temporal herniation. (A) Brain œdema without temporal herniation; third ventricle oblique. (B) Brain œdema and temporal herniation (X); third ventricle shifted *en masse*. Note a downward herniation of the hypothalamus (O).

The different clinical signs just described make the exact localization of brain tumours a difficult matter and render their prognosis most serious. The condition existing in temporal herniation may be aggravated by sudden increase of œdema by lumbar puncture or by ventri-

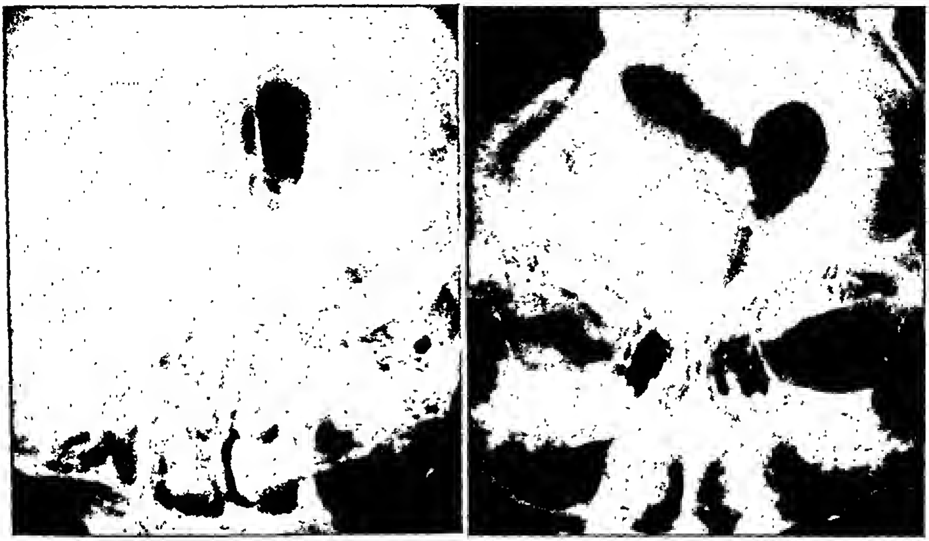


FIG. 3.—Ventriculograms. (A) No temporal herniation, third ventricle oblique. (B) Temporal herniation, third ventricle shifted *en masse*.

cular puncture on the normal side. The patient then becomes drowsy and comatose, stiffness of the neck increases, the heat-regulating mechanism is affected and there is visceral vasodilatation particularly affecting the lungs.

(*b*) *Infra-tentorial tumours.*—Tumours situated below the tentorium are frequently associated with brain œdema although the signs of such œdema are far less obvious than in those cases where it occurs above the tentorium. Displacement by a tumour, even a small one, may be rapidly followed by remote phenomena due to compression of the bulb and pons. The most revealing signs of such compression are stiffness of the neck, tendency to lateral inclination of the head and possibly decerebrate fits.

Œdema of the cerebellum has important anatomical consequences, with an increase of downward tonsillar herniation and the development of marked ventricular dilatation.

Cerebellar œdema rarely occurs in association with œdema of the cerebral hemispheres, the latter being found particularly in the brains of patients who have died following operation.

A particular complication of cerebral œdema occurs in cases of tumour and abscess situated in the upper half of the cerebellum in the form of an upward herniation of the cerebellum above the tentorium [5], producing at ventriculography a shift of the third ventricle which may lead to confusion and suggest the presence of a tumour in the posterior part of the third ventricle (fig. 4 *below* and fig. 5 *see p. 38*)

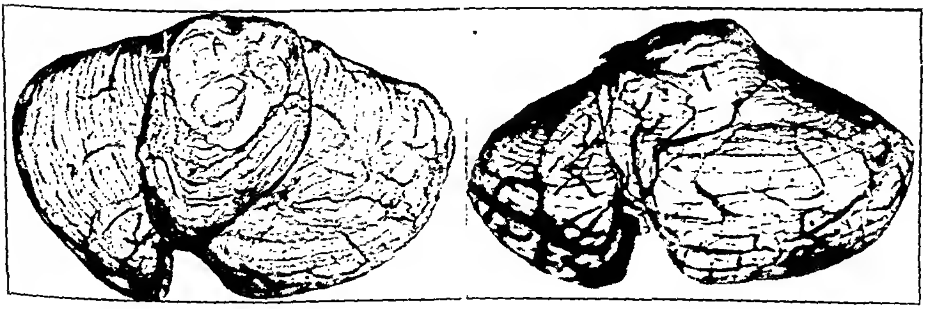


FIG. 4.—Upward cerebellar herniation. (A) From above. (B) From the side.

II.—ACUTE BRAIN ŒDEMA

(*a*) *Operative œdema*.—As described by one of us at the International Neurological Congress in London in 1935, the neuro-surgeon may see œdema developing during operations in the subfrontal region as for the removal, for example of a suprasellar meningioma. The œdema is seen as a tremendous swelling of the cerebrum which is solid and unassociated with change in blood-pressure. Should the patient die petechial hæmorrhages may be found disseminated throughout the frontal lobes.

Acute swelling of the cerebellum may occur during subtentorial operations, resulting from sudden compression or decompression; in such cases a marked rise of blood-pressure always precedes the œdema and is accompanied by dilatation of all the arteries.

(*b*) *Experimental œdema*.—This is an acute swelling of the brain produced by small traumatic lesions of the brain-stem (pons and crura). Most of this work was started at La Sorbonne [6], and was continued during 1942 at the National Institute for Medical Research, Hampstead with the support of the Medical Research Council (fig. 6).

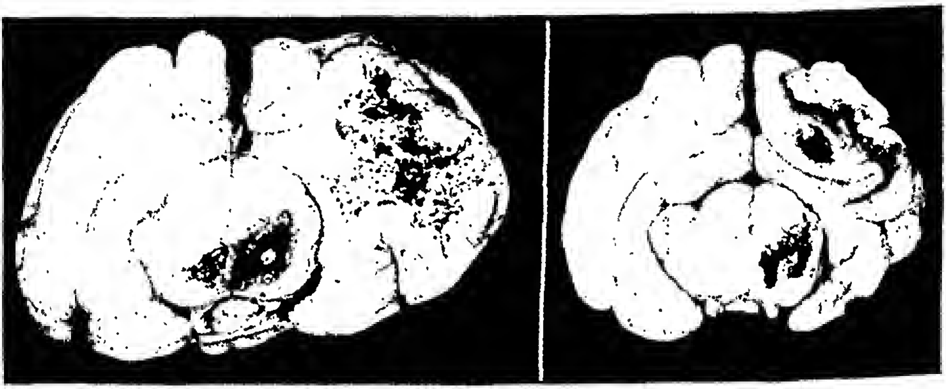


FIG. 6.—Cat. (A) Acute brain œdema from peduncular lesions.
(B) Peduncular lesion without acute brain œdema.

Such acute swelling is usually associated with a great increase in blood-pressure although this is not invariable. The occurrence of this swelling, associated with brain-stem trauma, we call *active* brain œdema and the mechanism of its production is still obscure.

(*c*) *Acute œdema in head injuries*.—We believe the occurrence of generalized œdema is frequent in cases of acute head injury and can be demonstrated by making supra-tentorial burrholes where swollen brain can be seen in the absence of a serious hæmorrhage. A possible cause for such œdema could be some lesion of the brain-stem as in the experiments mentioned above.

III.—CLASSIFICATION

Variations in morphology, ætiology and development (chronic or acute) in brain œdema may be analysed as follows:

(1) An œdema which appears to be the consequence of obstruction of the venous circulation, i.e. due to compression of veins and dural sinuses stretched and collapsed by high intracranial pressure. This circulatory defect when it reaches the intracerebral vascular pattern increases the cerebral swelling and thus creates a vicious circle.

(2) "Active œdema" which appears to be independent of a mechanical process and is due to vasomotor changes.

(3) Œdema in association with brain tumour depends in varying degree on one or other of the above-mentioned types:—

(*a*) Many brain tumours may develop pressure on the brain-stem which may produce "active œdema".

(*b*) Some large tumours may cause œdema through venous stasis which is relieved when the tumour is removed.

(*c*) Tumours, such as metastases, may produce "active œdema" quite out of proportion to the small size of the tumour.

IV.—TREATMENT OF CEREBRAL ŒDEMA AND ITS COMPLICATIONS

(*a*) The large decompressive flap has had much success especially for subacute œdema. It has been much employed for lesions requiring two-stage operations as, for instance, in cases of cerebral abscess, which are allowed to mature under decompression. The decompressive flap is less useful in cases of acute traumatic or infective œdemas because the dura stretches only very slowly. In addition the turning of a bone flap is by itself a trauma and may increase the œdema. The danger of cerebral œdema is not only related to the mechanical pressure on the brain but also to the swelling of the brain-stem whose functions may be altered or destroyed as a result of hæmorrhage.

(*b*) When it is impossible to remove the cause of brain œdema (as by excising a tumour) the best treatment remaining is the classic one of dehydration. For intracranial hypertension magnesium sulphates have given the best results and in some cases we inject as much as 240 c.c. in twenty-four hours at the rate of 20 c.c. every two, three or four hours.

The method of dehydration has replaced the decompressive bone flap and extensive experience has proved that it is safe. The important point is to establish through trephine openings the presence of cerebral œdema.

(*c*) Because of its practical importance the complication of temporal herniation in brain œdema has justified attempts at direct surgical treatment and such herniation should always be reduced at once if the patient's life is in danger. The best technique for reduction of temporal herniation seems to be "simple reposition" by the subtemporal route. The line of approach is in the plane passing through the external auditory meatus which lies between the two venous anchorages of the temporal lobe, the veins of Sylvius and Labbé. This has the advantage of exposing the middle portion of the tentorial incisura. When this point is reached the herniated convolution is lifted backwards with the production of an immediate flow of cerebrospinal fluid. We now as a routine, explore the Bichat opening when removing a tumour from the temporal region, reducing the herniation if it is present (fig. 7).

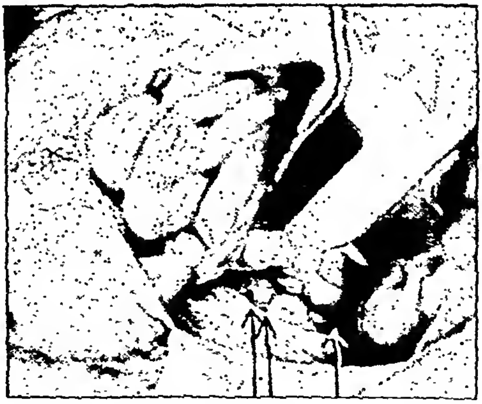


FIG. 7.—Surgical reduction of temporal herniation.
↑ Third cranial nerve. ↑↑ Free edge of tentorium.

For patients with other tumours showing temporal herniation we prefer to reduce the herniation at a second stage procedure if the patient does not recover after the primary removal of the tumour. If temporal herniation has not yet caused definite lesions in the brain-stem operative reduction improves the patient's condition and on the day following operation he is again conscious without headache or stiffness of the neck.

Our results support similar observations on the reduction of temporal herniation made by other surgeons and have convinced us of the importance of this manœuvre in the management of cases of brain tumour [1].

REFERENCES

1 GUIOT, G., et JANNY, P. (1947) Réduction Chirurgicale de la Hernie Temporale, *Sem. Hôp. Paris*, 23, 748-758.
2 JEFFERSON, G. (1938) The Tentorial Pressure Cone, *Arch. Neurol. Psychiat. Chicago*, 40, 857-876.
3 LE BEAU, J. (1938) L'Œdème du Cerveau. *Paris.*
4 —— (1943) L'Engagement du Lobe Temporal, *Un. méd. Can.*, 72, 761-762.
5 —— (1944) Hernie du Cervelet au dessus du Tentorium, *Un. méd. Can.*, 73, 243-252.
6 ——, et BONVALLET, M. (1938) Œdème Aigu du Cerveau par Lesion du Tronc Cérébral. *C. R. Soc. Biol. Paris*, **127**, 126-128; **129**, 833-836; (1939) **131**, 1128-1130.
7 VINCENT, C., DAVID M., et THIEBAUT, F. (1936) Cone de Pression Temporal, *Rev. neurol.*, 65, 536-545.

Professor Geoffrey Jefferson: Cerebral œdema cannot be regarded as an entity existing by itself because it is invariably secondary to something else, something affecting the brain primarily or else derived from some toxic or disordered state affecting the whole body in greater or lesser degree, but again with a local exciting cause.

I must speak of the condition as a clinician, as a neuro-surgeon in particular, concerned chiefly with brain tumours and infections of the central nervous system The ordinary methods of histology are not sufficiently informative to tell us all that we wish to know about œdema, except that it exists. It can say little directly of its causation except by inference. I should be on much firmer ground had I the authority to speak as a biochemist, for it is only by chemical researches that the missing answers can be found. I feel sure that neuro-pathologists would agree if in future we were to send three-quarters of any tumour that we remove to the biochemist and a quarter to themselves. It is just over sixty years ago that Thudicum published his famous "Chemical Constitution of the Brain" (1884) and thereby gave a sure starting place for further researches into the properties of the salts, proteins, sterols, fatty acids and those intensely hygroscopic substances, the cerebrosides, of which the brain is ultimately compounded. Researches have advanced our knowledge much further since those days and beginnings have been made in relation to cerebral œdema. But too much is still a matter for speculative inquiry, the exact causes so far largely escape us. Gross facts we certainly have. The observation that increase in brain volume is always greater than can be accounted for by the actual dimensions of a brain tumour or abscess is an old one. The overplus is œdema. I can see only two explanations: (1) that there are peculiarities in the osmotic pressure in the capillaries of tumours, or (2) that tumours shed toxic metabolites that affect the rest of the brain mass. The third possibility put forward by Dr. Le Beau is still *sub judice.*

On the first alternative, work that James Hardman did in my Unit some years ago seems to me suggestive. Using the Pickworth stain he demonstrated the extremely rich blood supply of malignant tumours, those in which œdema is most evident. True capillaries scarcely exist in these tumours; their place is taken by great numbers of sinusoids, which are neither capillaries, arteries nor veins and seem to be arteriovenous communications. These are impressive. Furthermore, in many operations on malignant tumours, veins may be seen leaving the tumour district filled with bright red blood. This could only be because either (*a*) the tumour is unable to abstract oxygen from the blood, or (*b*) that the arterial blood has been short-circuited in its way through the tumour. The latter, judged by Hardman's morphological studies, seems to be more probable and since we know that fluid exchange depends on intracapillary pressure and on the state of the capillary walls, it is possible that œdema might be the result of changes in hæmodynamics alone.

That this is not the only explanation seems to be certain from the fact that œdema occurs not only with actively growing tumours but with some that have a more ordinary internal vascular architecture, tumours that grow slowly and are, one might surmise, inert, e.g. many meningiomas. Sometimes a small anterior polar meningioma, neither of a size nor in a position where it could exert much pressure on the brain, is associated with a massive œdema of the ipsilateral hemisphere. What can be the cause except it be toxic? I conclude therefore that the cause of œdema is often toxic, although the exact kind remains to be discovered, but that it may be contributed to by capillary peculiarities in the tumours themselves. The toxic factor in infections is scarcely to be debated.

Œdema does not seem to be so serious a problem to the surgeon as it was twenty years ago. Or is it that it is less often invoked as an explanation of neurological disablement since we have learned better the nature of neuronal methods of working? In the main the clinical effects of cerebral œdema are mass effects showing themselves in tentorial or foraminal herniation in ways which the previous speakers have illustrated. This is a subject to which I have nothing much to add to what I wrote ten years ago. There is something, however, which should be said about the effects of œdema on nervous functions. It is not yet proven that œdema alone will block transmission either in axons or at synapses. It may do so, but we do not know that for certain. If it seems to do so, have we the right to assume that it is the œdema which is the active factor? I think not. When a neurone is swollen and is functionless the real reason for its paralysis must be the cause that made it swell. We know that thrombosis of a cerebral vein is often accompanied by swelling of a relevant area, great or small, and that, for example, a paresis may result. The reason is, surely, not because of œdema but because of disturbances of metabolism, of the supply of oxygen and other substances necessary for cell function. Œdema and paralysis are not to be taken, then, as a plain sequence of cause and effect; both are more likely to be due to a common factor which produced the two. My plea is for scepticism in our thinking until the truth is learned by experiment fortified by clinical observation.

Dr. J. G. Greenfield: *The problem of cerebral œdema in neuro-surgery* is a difficult one, not least because of the question of nomenclature and definition. The term *œdema* should properly be reserved for instances in which the excess of fluid in the brain is entirely interstitial. If such cases occur they are exceptional. In all the forms I have encountered there is some swelling of the tissue elements, especially those of the white matter. The term *brain swelling* was used by the older German writers to indicate intracellular swelling as opposed to interstitial œdema. But we do not know whether such a condition exists in a pure form since the artefacts necessarily accompanying fixation make histological differentiation impossible. The chemical evidence favours the supposition that most of the fluid is interstitial, at least in the œdema of cerebral tumours. It appears therefore that the two conditions are always associated. The excess of fluid is partly interstitial, but there is also swelling of the tissue elements. One word may therefore be used for the condition, and that of *cerebral œdema,* although perhaps not scientifically exact, is preferable both for euphony and distinction to that of *brain swelling.*

I do not include increase of fluid in the ventricles or subarachnoid space under the term "cerebral œdema" as I think that such a grouping tends to confusion.

Criteria of Cerebral Œdema

Various criteria have been suggested for œdema of the brain or brain swelling. The first was that of Reichardt who compared *brain volume* with *skull capacity.* A difference of less than 8% was held by him to indicate brain swelling. This criterion has recently been used by Alexander and Looney (1938), and by J. C. White and his associates (1943). It is assumed in using this criterion that no vascular lesions such as undue congestion, or hæmorrhage, exist. *Herniation* of the *hippocampal gyrus* between the incisura tentorii and the brain-stem, was used by Le Beau as his criterion, and up to a point it is a valid one, although difficult to estimate quantitatively. Recent work on œdema of the brain following burns by Walker and Shenkin (1945), and in the M.R.C. report on burns (1944) is also based on this criterion. Tonsillar herniation, or cerebellar coning, is less easily assessed. The *chemical criterion* of increased ratio of wet to dry weight of the brain, must be applied separately to white and grey matter as these have different normal ratios. In fact different areas of white matter normally show some variations in this ratio. Some of the American work on traumatic cerebral œdema was vitiated by a failure to recognize these differences. Stewart-Wallace has shown that an excess of sodium chloride in the tissues of the brain may also be a valuable criterion of œdema.

Finally there are the *histological criteria* to which I propose to devote most of my remarks.

(1) *Œdema in relation to cerebral tumours and abscesses.*—The histological changes seen in œdema of the brain surrounding tumours or abscesses were described by Jaburek in 1935 and I devoted a study to them in 1939. They consist in diffuse pallor of myelin staining in the centrum ovale on the side of the tumour, with comparative sparing of the subcortical fibres and of the larger commissural tracts such as the corpus callosum and the optic radiations. The pallor of staining is associated with irregular swellings on the myelin sheaths and axons. It was constantly associated with swelling of the cell bodies of the astrocytes, affecting all the astrocytes in the œdematous area, usually to a similar degree and in a similar manner. Where the œdema was severe, the change in the astrocytes might be of regressive nature, producing the amœboid glial cells described by Alzheimer and Spatz, or the clasmatodendrosis of Cajal. The nucleus was often pale or was shrunken and pyknotic, or its membrane was folded. In less damaged cells the nucleus was often enlarged along with the enlargement of the cell body. It might be reniform, and not infrequently showed mitoses. Intermediate

forms were not uncommon. In cases of œdema of longer standing there was evidence of increase in number of neuroglial fibres as well as of astrocytes. I could find no such constant change in the oligodendroglia but in acute and severe cases there was some swelling of the cell body. Later writers, however, have found some amœboid swelling of the oligodendroglia in the œdema surrounding cerebral tumours and Courville (1942) has seen the same change in traumatic œdema. There is always some spacing-out of the tissues, but only in the most severe examples is there any stainable interstitial fluid. This is probably because, as Professor Clovis Vincent has suggested, the fluid contains very little protein. I found no evidence of dilatation of perivascular spaces in the white matter but other writers, especially those who have used paraffin sections, have found this to be fairly constant. The cortex also was normal in the less severely affected cases which I studied. In one case the neurons of the fifth layer showed slight swelling resembling axonal reaction which may well have been secondary to the lesions in the underlying white matter. In another case more severe changes resembling those of ischæmia were present in the third layer. In cases of cerebral abscess, where the œdema was usually of more severe degree, degenerative changes in the cortical neurons were not uncommon. These were associated with swelling of the cortical astrocytes and proliferative changes in the microglia.

(2) *Traumatic cerebral œdema.*—(i) *Local form*: Œdema with similar histological characters is found in most cases of cerebral trauma in restricted zones which surround areas of bruising or hæmorrhage in a more or less concentric fashion. The width of this zone rarely exceeds 2 cm. In some of our cases, examined during the war years, there was also evidence of periventricular œdema. The outline of this zone shades off gradually, and in this respect differs from that of the areas of ischæmic degeneration of white matter, due to damage to the vessels entering it from the surface, which are commonly found in cases of cerebral trauma. In cases of cerebral hæmorrhage, traumatic or otherwise, the width of the zone of œdematous pallor usually varies with the size and to some extent with the duration of the hæmorrhage.

These histological changes in the white matter are so definite and characteristic that not only is it possible to say from the study of a section that œdema is present but also to estimate its degree and duration. There may, however, be forms of cerebral œdema, especially perhaps affecting the grey matter, in which a different histological pattern is seen, or in which the histological changes are so slight as to be recognized only by the most minute study.

(ii) *Diffuse traumatic œdema:* The occurrence of diffuse traumatic œdema is still a matter of dispute. Some authors, among whom I must include myself, have never seen it. Others consider it fairly common. Many of the chemical investigations which have been undertaken to prove its presence have, as I have indicated previously, been vitiated by using for examination material containing both grey and white matter, and are therefore valueless.

Experimental investigations are equally contradictory. Pilcher in his experiments in which he allowed weights of 500 and 1,000 grammes to fall on the heads of dogs from a height of 5 feet, could find no definite evidence of œdema. His experiments showed a gradual increase in cerebrospinal fluid pressure beginning in one to two hours after injuries with the kilogramme weight; this was associated with a very slight increase in water content in all parts of the brain. But this never exceeded 1-2%. White and his co-workers using pendulum blows on the heads of cats, after the method of Denny-Brown and Russell, also found a slight rise of cerebrospinal fluid pressure from the normal range of 55-90 mm. up to a range of 97-135 mm. From one hour to twenty-four hours after mild degrees of concussion, from which the animals appeared to have recovered completely, they found an increase in brain volume in relation to skull volume of 2% or 3% and in one case of 5·6%. They examined the brains of 20 cats histologically finding no evidence of cerebral congestion and only slight evidences of œdema, e.g. swelling of oligodendroglia cells, enlargement of perivascular and pericellular spaces, hydropic changes in the ependyma or vacuoles in the white matter, but none of these changes was found in more than 3 of the 20 brains, and most of them in only one or two. They can therefore be considered minimal or nugatory. What seems clear from this and earlier work by White and his collaborators is that an increase in size of the brain up to 5% or even more, need not be associated either with definite quantitative chemical or with obvious histological changes.

The experiments of Le Beau and Bonvallet indicated that œdema of the cerebral hemispheres might result from lesions of the brain-stem. There is a certain resemblance between these results and those of White and his collaborators seeing that blows given by the pendulum technique which they adopted produce demonstrable histological lesions only in the brain-stem (Windle *et al.*, 1944). The changes in the nerve cells of the cerebrum found by Del Rio Hortega in Le Beau's material were not found by myself in his later experimental material, but in any case they were slight, consisting only of swelling and occasional vacuolation of cytoplasm and eccentricity of nucleus of nerve cells, especially in the basal ganglia. They appear to me to be of doubtful significance.

Courville has recently supported the thesis that generalized cerebral œdema of the "dry brain" type may occur after trauma. He finds such brains congested on the surface. Histologically they show diffuse swelling of the oligodendroglia, with some increase in the number of these cells, at a later stage. Oligodendroglial swelling in his view precedes the formation of interstitial vacuoles in the tissue and may account for much of the increased volume of the white matter. He has also found widespread vacuolar changes of minor degree in the cortical nerve cells which resemble in some respects those seen in experimental hydration of the cortex. He considers, however, that generalized traumatic œdema is a rare condition, and he illustrates it with a photograph of a brain in which there are hæmorrhages in both lenticular nuclei which may well have contributed to the œdematous state.

The nature of cerebral œdema remains a mystery. There appears to be a double process, an increased permeability of the walls of the capillaries on the one hand, and a metabolic change leading to swelling of the tissues of the brain, especially those of the white matter, on the other. It is presumed that both may be caused by the same metabolic disturbance, e.g. alterations of hydrogen-ion concentration, anoxia, or the presence of toxic substances. This disturbance may come from the blood, resulting in generalized cerebral œdema as in the cases after extensive burns or scalds, and in those where it is secondary to disease of the liver or kidneys, or alterations in the hydrogen-ion concentration of the blood. Where the œdema is more localized we must suppose that the metabolic change or the toxic substance arises within the brain, e.g. in a bruised or infected area of brain tissue. In cases of cerebral tumour the œdema may be in this sense toxic, i.e. due to metabolites arising in the tumour—as is widely held—or it may be due to widespread ischæmia of the tissues resulting from the compression of the capillary bed or obstruction to venous outflow. Both factors may of course be at work. But it is clear from the distinction between areas of œdema and those of ischæmia in brain trauma, that we cannot consider anoxia as the only cause of œdema. That anoxia may cause swelling of the brain and histological changes some of which are similar to those seen in cerebral œdema is well known, but it seems necessary to postulate some other factor to account for other histological characteristics of cerebral œdema.

The fact that cerebral œdema is not entirely interstitial may account for its resistance to treatment with hypertonic solutions. Undoubtedly such treatment may relieve symptoms of intracranial pressure, but I believe that it does so by producing shrinkage of the brain as a whole, and not a disproportionate shrinkage of the œdematous area. This opinion is based on my observations in the œdema surrounding cerebral tumours, and I do not uphold it strongly in respect of other forms of œdema of which I have less experience. But I have seen no evidence that treatment with hypertonic solutions can directly and specifically affect the œdema surrounding cerebral tumours. The brain may shrink, but the œdema remains. The effect of this treatment is therefore at best temporary and palliative.

REFERENCES

Alexander, L., and Looney, J. M. (1938) *Arch. Neurol. Psychiat., Chicago*, 40, 877.
Le Beau, J. (1938) L'œdème du cerveau. Paris.
Bonvallet, M., and Le Beau, J. (1938-39) *C. R. Soc. Biol., Paris*, **127**, 126; **129**, 833; **131**, 1128.
Courville, C. B. (1942) *Bull. Los Angeles neurol. Soc.*, 7, 55.
Greenfield, J. G. (1939) *Brain*, 62, 129.
Jaburek, L. (1935) *Arch. Psychiat. Nervenkr.*, **104**, 518.
M.R.C. Report (1944) No. 249. Studies of Burns and Scalds.
Pilcher, C. (1937) *Arch. Surg., Chicago*, 35, 512.
Riehl, G. (1931) *Arch. Derm. Syph. Wien*, **164**, 409.
Spatz, H. (1929) *Arch. Psychiat. Nervenkr.*, 88, 790.
Walker, J., and Shenkin, H. (1945) *Ann. Surg.*, **121**, 301.
White, J. C., Brooks, J. R., Goldthwait, J. C., and Adams, R. D. (1943) *Ann. Surg.*, 118, 619.
Windle, W. F., Groat, R. A., and Fox, C. A., (1944) *Surg. Gynec. Obstet.*, 79, 561.

Dr. A. M. Stewart-Wallace: *The physico-chemical investigation of cerebral œdema* [Abstract].—The term œdema has a definite pathological meaning which has been defined as "an effusion of watery fluid into the intercellular spaces" and should therefore only be used to denote those conditions in which such an effusion is present. The problem that presents itself therefore is that of how to determine conclusively the presence of an increase of interstitial fluid in cerebral tissue. The severe œdematous tissue in the neighbourhood of cerebral tumours, with corresponding tissues from the opposite hemisphere as a control, seemed to offer good material for an analysis of the fluid changes.

By drying the tissue to a constant weight it was found (Stewart-Wallace, 1939, *Brain*, 62, 426) that the cortical grey matter (average 84·3%) contains considerably more water than the forms were not uncommon. In cases of œdema of longer standing there was evidence of increase in number of neuroglial fibres as well as of astrocytes. I could find no such constant change in the oligodendroglia but in acute and severe cases there was some swelling of the cell body. Later writers, however, have found some amœboid swelling of the oligodendroglia in the œdema surrounding cerebral tumours and Courville (1942) has seen the same change in traumatic œdema. There is always some spacing-out of the tissues, but only in the most severe examples is there any stainable interstitial fluid. This is probably because, as Professor Clovis Vincent has suggested, the fluid contains very little protein. I found no evidence of dilatation of perivascular spaces in the white matter but other writers, especially those who have used paraffin sections, have found this to be fairly constant. The cortex also was normal in the less severely affected cases which I studied. In one case the neurons of the fifth layer showed slight swelling resembling axonal reaction which may well have been secondary to the lesions in the underlying white matter. In another case more severe changes resembling those of ischæmia were present in the third layer. In cases of cerebral abscess, where the œdema was usually of more severe degree, degenerative changes in the cortical neurons were not uncommon. These were associated with swelling of the cortical astrocytes and proliferative changes in the microglia.

(2) *Traumatic cerebral œdema.*—(i) *Local form*: Œdema with similar histological characters is found in most cases of cerebral trauma in restricted zones which surround areas of bruising or hæmorrhage in a more or less concentric fashion. The width of this zone rarely exceeds 2 cm. In some of our cases, examined during the war years, there was also evidence of periventricular œdema. The outline of this zone shades off gradually, and in this respect differs from that of the areas of ischæmic degeneration of white matter, due to damage to the vessels entering it from the surface, which are commonly found in cases of cerebral trauma. In cases of cerebral hæmorrhage, traumatic or otherwise, the width of the zone of œdematous pallor usually varies with the size and to some extent with the duration of the hæmorrhage.

These histological changes in the white matter are so definite and characteristic that not only is it possible to say from the study of a section that œdema is present but also to estimate its degree and duration. There may, however, be forms of cerebral œdema, especially perhaps affecting the grey matter, in which a different histological pattern is seen, or in which the histological changes are so slight as to be recognized only by the most minute study.

(ii) *Diffuse traumatic œdema:* The occurrence of diffuse traumatic œdema is still a matter of dispute. Some authors, among whom I must include myself, have never seen it. Others consider it fairly common. Many of the chemical investigations which have been undertaken to prove its presence have, as I have indicated previously, been vitiated by using for examination material containing both grey and white matter, and are therefore valueless.

Experimental investigations are equally contradictory. Pilcher in his experiments in which he allowed weights of 500 and 1,000 grammes to fall on the heads of dogs from a height of 5 feet, could find no definite evidence of œdema. His experiments showed a gradual increase in cerebrospinal fluid pressure beginning in one to two hours after injuries with the kilogramme weight; this was associated with a very slight increase in water content in all parts of the brain. But this never exceeded 1-2%. White and his co-workers using pendulum blows on the heads of cats, after the method of Denny-Brown and Russell, also found a slight rise of cerebrospinal fluid pressure from the normal range of 55-90 mm. up to a range of 97-135 mm. From one hour to twenty-four hours after mild degrees of concussion, from which the animals appeared to have recovered completely, they found an increase in brain volume in relation to skull volume of 2% or 3% and in one case of 5·6%. They examined the brains of 20 cats histologically finding no evidence of cerebral congestion and only slight evidences of œdema, e.g. swelling of oligodendroglia cells, enlargement of perivascular and pericellular spaces, hydropic changes in the ependyma or vacuoles in the white matter, but none of these changes was found in more than 3 of the 20 brains, and most of them in only one or two. They can therefore be considered minimal or nugatory. What seems clear from this and earlier work by White and his collaborators is that an increase in size of the brain up to 5% or even more, need not be associated either with definite quantitative chemical or with obvious histological changes.

The experiments of Le Beau and Bonvallet indicated that œdema of the cerebral hemispheres might result from lesions of the brain-stem. There is a certain resemblance between these results and those of White and his collaborators seeing that blows given by the pendulum technique which they adopted produce demonstrable histological lesions only in the brain-stem (Windle *et al.*, 1944). The changes in the nerve cells of the cerebrum found by Del Rio Hortega in Le Beau's material were not found by myself in his later experimental material, but in any case they were slight, consisting only of swelling and occasional vacuo-

Section of Dermatology

President—SYDNEY THOMSON, M.D.

[*March* 20, 1947]

Parapsoriasis, Retiform Variety.—J. E. M. WIGLEY, F.R.C.P.

B. H., boy aged 9. First seen in February 1941 when the eruption was said to have been present two and a half years. He then had red, mottled areas affecting both legs and lower halves of thighs. There was some slight scaling over the erythematous areas and some hyperkeratosis about the knees and ankles. There was no complaint of irritation then and he seemed a perfectly healthy child otherwise. The eruption has been present both in summer and winter.

I saw him again in January 1947 when the lesions were said by his mother to have altered very little. It was then noted that the area of skin affected reached from about the junction of the upper and middle third of each thigh to the ankle. A small area on the side of his neck, below and behind each ear, and a similar small area on the under surface of the chin were affected. The lesions on the legs present a striking appearance. The whole area is slightly scaly and made up of gyrate narrow bands of erythema producing a figurate appearance recalling that shown by the condition known as erythema ab igne. The scaling is dry and thin and the skin between the erythematous lesions gives some impression of false atrophy. The lesions about the neck and chin are simply dry and scaly and do not show the arabesque figures present on the legs. There are a number of scaly papules scattered over the arms.

The eruption irritates slightly on exposure to heat.

Wassermann and Kahn reactions are negative.

Histological examination (Dr. Muende).—"Beyond a vacuolation (desiccative) of the superficial layers of the stratum corneum and a slightly increased cellular infiltration in the neighbourhood of the superficial capillaries, there are no pathological features suggestive of any specific skin condition."

The condition appears to me very characteristic of that described by many authorities as parapsoriasis lichenoides and grouped by Dr. MacLeod (*Brit. J. Derm.* (1943), 44, 569) as the reticulate variety. MacLeod mentions the occasional resemblance to erythema ab igne. The only really unusual feature seems to me to be the extreme youth of the patient at the onset.

Dr. F. Parkes Weber: The only objection that I should make to this description is the use of the term "retiform". Parts of the body may show this appearance, but the most typical parts of the thighs show a linear distribution of the dermatosis. I would suggest, considering the boy's age and the history that he gives of having had this condition ever since he can remember, that the case is really a *forme fruste* of a congenital ichthyosiform erythrodermia.

Acne Conglobata.—L. FORMAN, M.D.

W. W., aged 20. At the age of 16 he was 6 feet tall, plump, with well-developed penis and testicles. The hair growth was profuse over the face and limbs. The skin was intensely seborrhœic over the face, chest, and back. The striking clinical feature during the period of observation has been the development of large abscesses in the axillæ and perianal area involving the buttocks. The abscesses develop slowly, commence in the deep layers of the dermis, and may reach a size of 1 to 1½ in. across. They communicate with each other and, after discharging, heal leaving epidermal bridges. The depth of the abscesses and the absence of comedones raise the possibility of the infection occurring in the apocrine glands.

white matter, both of the cerebral (70·7%) and the cerebellar (70·6%) hemispheres, while intermediate values are found for the thalamus (75·1%) and corpus callosum (75·7%).

The total water content of seven specimens of œdematous cerebral tissue was determined and contrasted with corresponding tissue from the opposite hemisphere. It is perhaps worth pointing out here that in spite of the wet appearance of the œdematous brain, fluid does not actually drip or run from it as is often stated. All methods of draining, suction, filtering and squeezing failed to separate any fluid for analysis. A marked increase was found in the water content of the white matter on the side of the lesion (average 81·8%) compared with tissue taken from the opposite side (average 69·6%). There was no material difference between the grey matter of the cortex on the two sides. Moreover a more detailed analysis in three of the cases suggests that the changes are restricted to the centrum ovale and do not involve the corpus callosum, internal capsule or thalamus. These figures indicate a considerable addition of extra fluid in the œdematous white matter—an average addition of 59·1 c.c. per 100 grammes of whole tissue.

Since interstitial fluid contains a large amount of chloride and sodium and a very small amount of potassium and phosphate (the former being the principal extracellular ions and the latter the chief intracellular ions), an analysis of these electrolytes in tissue from the œdematous and normal hemispheres was carried out with a view to determining whether this additional fluid represents a simple increase of the interstitial fluid or some more complicated fluid change involving the cellular tissue. There is a very large increase in the amount of Cl in the œdematous tissue compared with the normal (average 29·6 milli-equivs % and 7·6 milli-equivs % respectively), a large increase in the Na (58·9% and 27·0% respectively, a negligible change in the K (22% and 21·3% respectively). In the grey matter, in which it has been shown that no change in the fluid content occurred, analysis of these electrolytes showed no significant change in the two cases examined. From these figures, showing the difference between the water and electrolytes on the two sides, the electrolytic composition of the additional fluid can be calculated and compared with serum.

	Na	Cl	K	Na/Cl ratio
Serum filtrate.. ..	14·8	11·1	0·25	1·33
"Œdema fluid" ..	13·3	9·2	0·21	1·44

It is thus shown that the electrolytic composition of the œdema fluid, determined in this way, closely resembles that of serum filtrate, and has therefore the same composition as lymph, serous transudates and œdematous fluid elsewhere in the body, and interstitial tissue generally. This demonstrates clearly that the cerebral œdema associated with cerebral tumours is an extra-cellular effusion derived from the blood plasma. Identical changes were found in one case of œdema associated with a recent cerebral hæmorrhage. It is almost certain, therefore, that local œdema in the neighbourhood of traumatic contusion of the brain is of the same nature.

It is felt that these experiments suggest that further biochemical investigation of biopsy and autopsy specimens of cerebral tissue would contribute to our knowledge of the occurrence and nature of cerebral œdema.

(A full account of this joint meeting will be published in *La Revue Neurologique*.)

Section of Dermatology

President—SYDNEY THOMSON, M.D.

[*March* 20, 1947]

Parapsoriasis, Retiform Variety.—J. E. M. WIGLEY, F.R.C.P.

B. H., boy aged 9. First seen in February 1941 when the eruption was said to have been present two and a half years. He then had red, mottled areas affecting both legs and lower halves of thighs. There was some slight scaling over the erythematous areas and some hyperkeratosis about the knees and ankles. There was no complaint of irritation then and he seemed a perfectly healthy child otherwise. The eruption has been present both in summer and winter.

I saw him again in January 1947 when the lesions were said by his mother to have altered very little. It was then noted that the area of skin affected reached from about the junction of the upper and middle third of each thigh to the ankle. A small area on the side of his neck, below and behind each ear, and a similar small area on the under surface of the chin were affected. The lesions on the legs present a striking appearance. The whole area is slightly scaly and made up of gyrate narrow bands of erythema producing a figurate appearance recalling that shown by the condition known as erythema ab igne. The scaling is dry and thin and the skin between the erythematous lesions gives some impression of false atrophy. The lesions about the neck and chin are simply dry and scaly and do not show the arabesque figures present on the legs. There are a number of scaly papules scattered over the arms.

The eruption irritates slightly on exposure to heat.

Wassermann and Kahn reactions are negative.

Histological examination (Dr. Muende).—"Beyond a vacuolation (desiccative) of the superficial layers of the stratum corneum and a slightly increased cellular infiltration in the neighbourhood of the superficial capillaries, there are no pathological features suggestive of any specific skin condition."

The condition appears to me very characteristic of that described by many authorities as parapsoriasis lichenoides and grouped by Dr. MacLeod (*Brit. J. Derm.* (1943), 44, 569) as the reticulate variety. MacLeod mentions the occasional resemblance to erythema ab igne. The only really unusual feature seems to me to be the extreme youth of the patient at the onset.

Dr. F. Parkes Weber: The only objection that I should make to this description is the use of the term "retiform". Parts of the body may show this appearance, but the most typical parts of the thighs show a linear distribution of the dermatosis. I would suggest, considering the boy's age and the history that he gives of having had this condition ever since he can remember, that the case is really a *forme fruste* of a congenital ichthyosiform erythrodermia.

Acne Conglobata.—L. FORMAN, M.D.

W. W., aged 20. At the age of 16 he was 6 feet tall, plump, with well-developed penis and testicles. The hair growth was profuse over the face and limbs. The skin was intensely seborrhœic over the face, chest, and back. The striking clinical feature during the period of observation has been the development of large abscesses in the axillæ and perianal area involving the buttocks. The abscesses develop slowly, commence in the deep layers of the dermis, and may reach a size of 1 to 1½ in. across. They communicate with each other and, after discharging, heal leaving epidermal bridges. The depth of the abscesses and the absence of comedones raise the possibility of the infection occurring in the apocrine glands.

To-day, pustular acne is still present over face and trunk. The axillæ show indurated areas with epidermal bridges, and granulomatous ridges covered with pyogenic membrane. The buttocks and perianal area are peppered with projecting granulomata and the sites of sinuses, and the area is generally indurated.

Cultures from unbroken abscesses have grown acne bacilli alone, or scanty *Staphylococcus albus* (hæmolytic) and *Staphylococcus aureus.* No tubercle bacilli were seen. Section of the wall of a buttock abscess showed a chronic granuloma with no evidence of tuberculosis.

The causal relationship of the acne bacillus in these abscesses is still undetermined. Cultures of acne bacilli rubbed over the back of this patient did not produce any signs of follicular reaction.

With regard to recent endocrine therapy for acne, in my experience with severe acne, small doses of œstrogens by mouth are ineffective. Implantation of the synthetic œstrogens, in addition to causing enlargement of the breasts and loss of libido, may have a definite inhibitory action on the pituitary and indirectly on the gonads.

Investigations have been reported on the effects of œstrone and œstradiol implanted as compressed tablets of pure hormone under the skin of male rats and mice. Inhibition of some of the functions of the pituitary gland were observed, with depression of the growth rate and shrinkage of the gonads.

There are also the possible psychological effects to be considered on potentially bisexual adolescents.

Pringle's Disease (Adenoma Sebaceum).—Hugh W. Gordon, M.C., M.B.

The patient, aged 14 years, was noticed two years ago to be developing red spots on the face. These were treated at St. John's Hospital for Diseases of the Skin with an "electric needle" and were said to improve very considerably. They have, however, reappeared during the last four to six months.

The patient is one of five brothers, and there is no history of the complaint in any other member of the family. He is said to be a little backward at school, but is in every other way perfectly normal.

On examination.—A large number of small papules are present on the cheeks and round the alar nasal folds with a well-marked telangiectatic element.

Dr. Gordon said that the patient appeared to be that rather uncommon phenomenon, the perfect textbook case of the disease. He was showing him for this reason and also for possible advice in regard to treatment. He was proposing to cauterize all the lesions thoroughly under a general anæsthetic.

Dr. Freudenthal: I would suggest that thorium X be tried.

Mycosis Fungoides.—Hugh W. Gordon, M.C., M.B.

The patient, a previously healthy man of 67, has noticed an abnormal thickening of the skin on his back for three years, which has slowly increased in size. Subjective sensations have been slight. During the last three or four months he has noticed a slight swelling in both armpits. His general health has been unimpaired.

On examination.—There was a sharply marginated plaque about 5 cm. × 4 cm. raised in the centre about a cm., the increase in thickening tapering off towards the edges, which have a waxy look.

The colour is purplish, the surface shiny with no suggestion of ulceration or granulation.

There is an enlarged gland in each axilla, and glands are slightly enlarged in both groins.

When first seen two months ago, a tentative diagnosis of mycosis fungoides was made with possible alternatives of Bowen's disease or a primary sarcoma. A section taken from the centre of the lesion on that occasion was reported on by Dr. Freudenthal as excluding Bowen's disease, but no diagnosis was possible on account of the high degree of chromatotaxis.

One X-ray treatment, dose 350 r was given to the lesion and to both axillæ.

On 18.2.47 considerable flattening had occurred which has, however, not persisted.

Another section taken on 5.3.47 shows a profuse cellular infiltrate with pleomorphism typical of mycosis fungoides.

Blood-count normal. The Wassermann test was negative.

Dr. Gordon added that the diagnosis of this condition rested almost entirely on the histology which he felt excluded everything other than reticulosis. The response to X-ray had been disappointing but he proposed to give a further X-ray with higher voltage.

Postscript (1.5.47).—Under high-voltage therapy the glands have completely regressed but the main lesion in the back has shown disappointing response.

Dr. W. Freudenthal: The friability of cells which Dr. Gordon met in his first biopsy, is, in my experience, frequently seen in mycosis fungoides and in other conditions of the reticulosis group, including the leukæmias: I look upon it as a diagnostic help. I have met it also fairly frequently in lupus erythematosus, which may be more than a coincidence.

Dr. P. J. Feeny: The fact that this case did not respond to a dose of X-rays points very much against the diagnosis of mycosis fungoides.

Dr. L. Forman: Would Hodgkin's disease be considered? Solitary cutaneous plaques have been described in this disease.

? Erythema Multiforme.—C. H. WHITTLE, M.D.

M. B., woman aged 24, a shorthand typist.

History of swellings on the lower posterior third of the legs for twelve weeks. She had a similar but much milder attack the previous winter.

Family history.—A brother has chronic red spots on his face (not seen).

The lesions consisted of two bluish-red circular infiltrated plaques 5 cm. in diameter with sharp edges raised above the surface of the surrounding skin on inner and posterior aspect of left ankle. There were several more recent lesions on the right ankle, posterior aspect, up to 1 cm. in diameter. They have an elastic almost rubbery feel and are slightly tender. At first glance they look like large blisters, with a yellowish translucent character. The larger plaques have resolved leaving bluish-brown discoloration. The remaining lesions are superficially reminiscent of colloid milium.

X-ray of chest: No evidence of disease. Mantoux reaction: Human and bovine 1 : 1,000 both positive. The sites of intradermal inoculation showed ten days or so later an increase in size and redness which has gradually subsided.

Wassermann reaction negative.

Biopsy.—There is an intense inflammatory perivascular and perifollicular exudate in the corium. The cells are chiefly small round cells and polymorphs. The clear yellow zone visible to the naked eye appears to be due to œdema and/or degeneration of colloid type in the papillary and subpapillary layers, which are thickened. No amyloid or mucin present. The epidermis is flattened and the rete pegs much diminished. The changes do not suggest tubercle or sarcoid, but might fit with the diagnosis of erythema multiforme.

Dr. F. Parkes Weber: Possibly this might turn into a case of erythema induratum; it might be an early form of that condition, although the microscope does not seem to support that view.

Congenital Ichthyosiform Erythrodermia (Brocq).—IAN MARTIN SCOTT, M.D.

Miss J. H., aged 17 years.

History.—Two weeks after birth the skin of the wrists became dry and cracked, and shortly afterwards this condition became generalized. Her mother did not notice any undue reddening of the skin, and treated her with daily baths of olive oil.

The condition has continued throughout her life, but she has noticed a gradual improvement during the past ten years. The skin has never blistered.

At the age of 8 years she was advised to wear spectacles for a slight visual defect, and possibly also for her bilateral ectropion.

She prefers cold weather; in warm weather she becomes intensely hot, and only sweats slightly from the palms, soles, axillæ and central portions of her face. With variations of external temperature she takes a longer time to become warm or to cool down than normal people.

On questioning, she states that her nails seem to grow more quickly than normal, but in contrast her hair seldom needs to be cut. The patient has always had moderate dandruff and washes her hair every week. Her teeth have always required much attention. Desquamation inside the auditory meatus causes occasional discomfort. The skin does not cause irritation during her working day, but in the warmth of bed is slightly itchy. She anoints herself with an emollient each night after her bath. She enjoys good general health, but occasionally suffers from sore throats, chilblains, and slight rheumatism of the shoulders and hips.

Family history.—The patient has a younger brother who is normal in all respects. There is no consanguinity of her parents, and none of her immediate relatives has ichthyosis.

Past health.—At the age of 7 years she had a mild attack of chicken-pox, but cannot describe the eruption. At 8 she had measles and then whooping cough. The measles rash caused a general desquamation which was very slow in the neck. Her tonsils were removed at the age of 10.

Present condition.—General systemic examination reveals no abnormality. Menstruation is of normal duration and rhythm. The teeth are sound and well cared for. The nails appear normal. The hair is of normal texture, but there is moderate dandruff.

The skin.—There is general dry scaling of the skin, which also involves the folds covering the large joints. Erythrodermia is seen to a moderate degree on the face and ears, and is well marked around the knees and elbows.

Detailed examination of the skin: The skin of the face is taut, parchment-like, and shows fine scaling. On the posterior and lateral aspects of the neck it is of more horny consistency, and greyish-brown. This type of skin extends into both axillæ, where there is little growth of hair.

Quadrilateral scaling is present on the limbs, and there is marked reddening over the elbows, wrists, and knees. The palms are moist and the skin of more normal texture with slight peeling at the joint flexures. The skin of the soles appears normal except for several callosities and a wart.

On the breasts the skin is pink and of fine parchment-like texture—it appears as though painted with a film of clear varnish and then cracked into quadrilaterals.

The skin of the abdomen is hyperkeratotic and yellowish-green. The hair of the pubic region is scanty. On the back the skin is dry and light brown; over the buttocks there is quadrilateral scaling with red lines between the scales.

Histology (8.2.47).—Biopsy from the right anterior axillary fold. The surface of the skin is irregular. The epidermis including the horny layer forms depressions, at the deepest parts of which the rete pegs are flattened; at the elevations the rete pegs are thickened. There is a well-marked hyperkeratosis consisting chiefly of compact horn, and no parakeratosis. The keratohyalin layer is thickened up to three to five layers in some places. There is patchy acanthosis, and in some places the rete pegs are elongated. In the papillary layer there is moderate œdema, and a slight perivascular infiltration of lymphocytes and fibroblasts. A small number of lanugo hairs with associated sebaceous glands are to be seen. The eccrine sweat glands are numerous and appear normal. In some places the blood-vessels are rather numerous, and the cells of the endothelial lining are swollen and conspicuous.

Comments.—So far as I am aware no similar cases have been published in this country since 1928. The principal features of this present case, which conform with those originally described by Brocq, are as follows: Onset within two weeks of birth; long duration; erythrodermia, most marked around the large joints; general ichthyosis, which includes the large joint folds; and a seborrhœic condition of the scalp.

Brocq also mentioned the following inconstant features: (*a*) Hyperkeratosis of the palms and soles—not present in this case. (*b*) Rapid growth of hair and nails—not a marked feature in this case.

The disease has been divided into two types depending on the presence of bullæ; there is no history of bullæ in this girl.

In addition to the essential features of the condition this patient also has a bilateral ectropion. It is of interest to note that in two of the three cases where there were no bullæ, in Brocq's original paper, bilateral ectropion was present, although not stressed by him as a feature of the disease. A further two cases showing bilateral ectropion have been described more recently.

I should like to record my thanks to Dr. W. N. Goldsmith for kindly allowing me to present this case.

Myxœdema Papulosum.—BERNARD GREEN, M.R.C.S., L.R.C.P., and W. FREUDENTHAL, M.D.

Mrs. M. D., aged 72.

In good general health. First noticed a "group of pimples" on the antecubital fossæ, the inner aspects of the arms and on the back of the neck. These all appeared eighteen months ago (October 1945) and are symptomless. She had a similar eruption about August 1944 which disappeared when she was treated for an attack of sciatica in February 1945, and remained clear for several months.

Past history.—In January 1943 she had a tumour on the left side of her neck, immediately below the angle of the jaw, the nature of which she does not know. Radium was used for treatment. She has varicose veins, ulcers and eczema of legs.

General examination.—A well-nourished woman of healthy appearance. Blood-pressure 200/100; other systems apparently normal.

Skin examination.—There are a large number of closely aggregated, non-confluent skin-coloured papules, 1 to 3 mm. in diameter, in both antecubital fossæ, (fig. 1) flexor aspects of the forearms, inner aspects of the upper arms extending along the anterior and posterior axillary folds and on the shoulders extending along the sides of the neck. There are also a number of grouped papules on the lower part of her back on either side of the intervertebral sulcus. She has slight perniosis on the posterior aspects of the upper arms, varicose veins and pigmented scars from healed ulcers on the ankles.

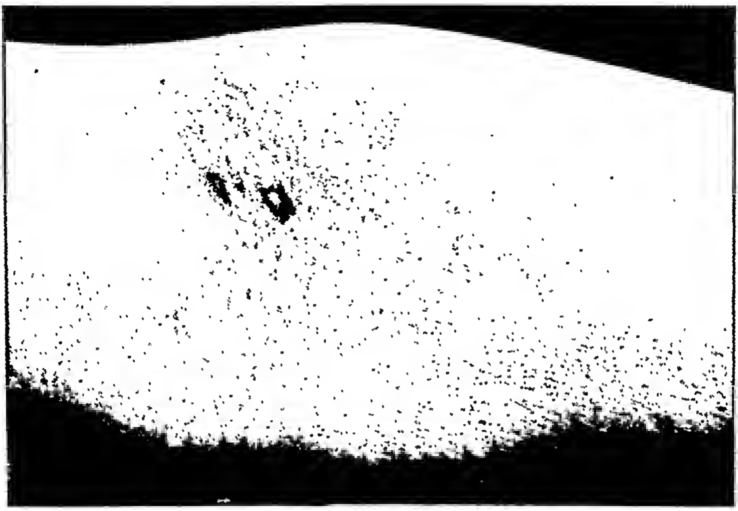


FIG. 1.—Myxœdema papulosum.

Biopsy.—Three discrete papules, arranged in a line, from the right upper arm, were excised. In the sections these papules show as well-defined round or oval areas in the middle and lower third of the cutis. They contain lymphocytes and fibroblasts and, chiefly in the central parts between the collagen bundles, thin strands of fibrinoid masses stained yellow with van Gieson; the elastic fibres are slightly diminished. The lymphocytes are mainly found towards the periphery of these areas and often arranged around small vessels. Each of these areas contains a small to moderate amount of mucin, forming a fine network that stains metachromatically pink with thionin.

The exhibition of tab. thyroid grain ½ t.d.s. was not well tolerated, but one tablet daily made her feel well; this did not influence the eruption.

Comment (B. G.).—I made a tentative diagnosis of pseudoxanthoma elasticum, which, however, was not confirmed by biopsy. I made an alternative diagnosis of myxœdema papulosum, and asked Dr. Freudenthal to make a biopsy.

A similar case, showing papular and annular lesions, was shown at this Section by Drs. Freudenthal and Brünauer in January 1942 (*Proc. R. Soc. Med.*, 35, 388).

Trotter and Eden (*Quarterly Journal of Medicine*, 1942, 35 (N.S. 11), 229) described cases of localized pretibial myxœdema in association with toxic goitre and summarized their findings in a series of cases and discussed the local and general factors governing the deposition of mucin in the skin. It would appear that this type of eruption of the skin occurs both in hypothyroidism and thyrotoxicosis and the condition is unaffected by the administration of thyroid extract or thyroidectomy. It would seem, therefore, that these cases are a form of dysthyroidism due to an overactivity of the pituitary gland.

Cases of pretibial myxœdema have been shown at this Section by Bamber, Forman and others. Dowling (*Proc. R. Soc. Med.*, 1934, 27, 1361), when showing a case, mentions another in which the lesions of the skin appeared several years before the onset of typical symptoms of Graves' disease.

Dr. W. Freudenthal: Three groups of cases of myxœdema may be distinguished: (1) The generalized myxœdema of cretins; (2) The pretibial myxœdema in Graves' disease of which Trotter and Eden have made a careful critical study (*Quart. J. Med.* 1942, 35 (N.S. 11), 229); (3) The "atypical" myxœdema (Jadassohn-Doessekker, *Arch. Derm. Syph., Wien*, 1916, 123, 76) which was the subject of a discussion at this Section in January 1942 when a case with papular and annular lesions in a patient with nodular goitre was shown (*Proc. R. Soc. Med.*, 35, 388). To this group belong the present case, the case with papular and plaque-like lesions (after thyroidectomy) shown at this Section in December 1946 (*Proc. R. Soc. Med.*, 1947, 40, 258); also Mumford and Barber's case of myxœdema moniliforme, shown January 1943 (*Proc. R. Soc. Med.*, 36, 286).

This third group deserves our attention and careful investigation, expecially from the endocrinological point of view.

Dr. W. R. Trotter: I agree with Dr. Freudenthal that we are here dealing with three quite separate conditions which affect the skin. There is first generalized myxœdema—hypothyroidism. Then pretibial myxœdema, which is invariably associated with a toxic goitre, although it may not appear until after the toxic goitre has been treated by thyroidectomy; nevertheless, it always appears in association with a toxic goitre. Finally there is the third group of which the present case is a good example. One would like to find some association with thyroid disease, but so far there is no direct evidence. Here, I think, we have to beware of falling into a terminological trap, for the term "myxœdema" is used in two quite separate senses, namely, the sense commonly used in general medicine for the clinical picture produced by deficiency of thyroid secretion, and the literal sense in which it is used in dermatology for a mucinous infiltration of the skin. In this connexion I think the dermatologists have the right on their side, and if we could choose the sense in which the word is to be used it would be better if the term "myxœdema" were kept for use in its literal sense. However, I am afraid things have gone too far, and the term "myxœdema" is in such common use in the sense of hypothyroidism that there is no hope of recalling it. But as long as the term is used in two different senses there will continue to be a considerable amount of confusion. All we can say is that in Dr. Freudenthal's third group none of the cases has responded to oral thyroid extracts. That is certainly true of the pretibial type also, and they are unaffected by thyroidectomy. Only in the first group, associated with hypothyroidism, does the skin change at all when thyroid extract is administered. At the moment the third group remains a baffling and extremely interesting problem.

Dr. Freudenthal: Could the pituitary gland play a role in these conditions?

Dr. Trotter: All we can say in that connexion is that pituitary over-activity may occur and may be a common factor linking the cases of hypothyroidism and the cases of pretibial myxœdema and toxic goitre, but again I have nothing to say about the third group.

Dr. E. Lipman Cohen: The name "pretibial myxœdema" is becoming so firmly entrenched as descriptive of a group that it is liable to be misleading if it is taken too exclusively. Lesions have been found on the lower part of the abdomen and on the thighs. I have suggested the name "myxœdema circumscriptum thyrotoxicum".

Dr. Freudenthal: As long as so much uncertainty exists as to the pathogenesis of all three groups of myxœdema it may be best to keep this term and use it simply as a descriptive one. Or, we may try to introduce the term "mucinoses" to cover all conditions in which the presence of mucin is an esssential factor; it may include granuloma annulare (*Proc. R. Soc. Med.* 1945, 38, 333).

Sarcoidosis.—BERNARD GREEN, M.R.C.S., L.R.C.P., and C. W. F. MCKEAN, M.B.

Mrs. M. L., aged 41. Two children. In good general health. The eruption first commenced on her legs and forehead eight years ago. She now presents a striking appearance. On the forehead there are gyrate brownish lesions with a slightly elevated scaly edge, the centre being smooth and slightly atrophic. There are also several reddish-brown nodules on the face, and irregular infiltrating purplish and brownish plaques on the upper and lower limbs and shoulders. All the lesions are symptomless.

The eruption was not influenced during pregnancy.

Her brother died of pulmonary tuberculosis five years ago.

A biopsy was done and the section shows some granulomatous tissue in the dermis. The lesion consists of round aggregations of endothelial cells with an occasional foreign-body giant cell. There is no evidence of caseation, and the Ziehl-Neelsen film shows no tubercle bacilli to be present.

W.R. is negative. Mantoux test negative. E.S.R. 27 mm. in first hour (Westergren). A skiagram of the chest shows slight enlargement of the right upper mediastinal glands, but no pathological changes in the lungs. A skiagram of the bones of the hands reveals nothing abnormal.

Dr. Hugh Gordon: The lesions on this patient's face are similar to those of a patient of mine shown to the Section in January. She has two circular plaques on the right lower arm with raised edges and a scaly atrophied centre. The histology was that of a sarcoid. In this present case there are both these superficial scaly lesions with scarring present together with the more typical indurated lesions on the limbs.

Dr. Gordon said that he had not previously seen this superficial scaly type of scarring though there was an excellent picture in Jadassohn's Handbook. His case was improving satisfactorily on calciferol.

Dr. C. H. Whittle: I should like to ask whether it is a frequent experience to see scarring in sarcoids. One has the opportunity of watching the course of very few cases of sarcoidosis, because they are rare, but in my experience resolution is not usually accompanied by atrophy.

Epidermolysis Bullosa Dystrophica.—C. W. F. McKean, M.B.

Irene M. P., aged 13 years 11 months.

On examination.—Admitted to the South Eastern Hospital for Children suffering from a bullous eruption involving especially the elbows, extensor surfaces of the forearms and hands, the abdomen, lower spine and buttocks, the thighs, legs and feet, also slightly the shoulders, neck and scalp. The bullæ were in all stages. Some contained serum, and some were hæmorrhagic. The epidermis between the bullæ in the more severely affected parts was extremely atrophied. There were many milia-like epidermal cysts, especially on the loins and extensor surfaces of the forearms. All the finger- and toe-nails had been lost. Her hair was fine and sparse, though her mother considered it to be thicker than ever before. Her teeth were soft and very badly decayed, many almost completely lost. Her tongue was small and shiny, with patches of leukoplakia, and could not be protruded beyond the teeth. Though of good average height, she was painfully thin. Finally, it was interesting when dealing with one congenital abnormality to find another, namely, that the right first and second toes were conjoined.

History.—She was born at home, weighing between six and seven pounds. After birth the right foot was found to be denuded of the epidermis, and at 3 weeks of age she was first brought to the hospital. She has been brought regularly every Thursday ever since, till the war began, and then she was evacuated with her mother, who cared for her till she returned to the hospital last month. Her notes go back to the age of 4, and the condition has remained much the same throughout. The birth injury to the foot healed quickly, but within the first seven days of life blisters were seen on the fingers, and thenceforth any knock or rub would cause a blister to develop. She is said to have been forward rather than backward with her teeth, and with walking and talking. She was fairly fat as a baby, but has been thin ever since she began to walk. She has never been to school, and was never allowed to play with other children. Having been taught solely by her mother and sister, it is a little hard to judge of her intellectual capacity. She reads children's books, writes interesting letters, and has a good memory.

Family history.—The parents are not related, and there is no history of any similar skin disease in the family. But her father exhibits transposition of the viscera. He also suffers from a gastric ulcer. There are no other familial congenital abnormalities.

Pathological investigations.—Wassermann and Kahn reactions negative. Urine: No porphyrins observed. Biopsy of blister (Dr. I. Muende): The epidermis has separated from the corium at the epidermo-dermal junction.

Treatment.—In the absence of specific treatment: confinement to bed, and penicillin dressings to prevent infection. The bullæ continue to arise, particularly with skin contact, for instance where the legs are crossed during sleep.

Discussion.—Epidermolysis bullosa usually begins during the first two years of life, and may subside at puberty. It is more frequent in males. It is divided into simple and dystrophic types, with intermediate cases. The simple type does not often affect the mucous membranes and does not leave scarring, nor are the nails affected. In the severe form the nails show many dystrophic changes, but are not often all lost.

The simple form is said to be inherited as a dominant, whereas the dystrophic may be as a dominant or recessive, the severest cases being recessive.

Senear-Usher Syndrome.—E. Colin Jones, M.B.

Miss I. R., aged 57, states that her skin trouble began in March 1946, with numerous blisters over the back, followed very shortly by similar lesions over the whole body—the outbreak coinciding with an attack of lumbago.

Initially she was treated with sulphanilamide ointment but the various areas were aggravated.

When first seen by me in July 1946 the condition resembled dermatitis herpetiformis. Irritation was marked, but potassium iodide patch test was negative. There was no response to either arsenic or tablets of M & B 693.

Dr. W. Freudenthal: Three groups of cases of myxœdema may be distinguished: (1) The generalized myxœdema of cretins; (2) The pretibial myxœdema in Graves' disease of which Trotter and Eden have made a careful critical study (*Quart. J. Med.* 1942, 35 (N.S. 11), 229); (3) The "atypical" myxœdema (Jadassohn-Doessekker, *Arch. Derm. Syph., Wien*, 1916, 123, 76) which was the subject of a discussion at this Section in January 1942 when a case with papular and annular lesions in a patient with nodular goitre was shown (*Proc. R. Soc. Med.*, 35, 388). To this group belong the present case, the case with papular and plaque-like lesions (after thyroidectomy) shown at this Section in December 1946 (*Proc. R. Soc. Med.*, 1947, 40, 258); also Mumford and Barber's case of myxœdema moniliforme, shown January 1943 (*Proc. R. Soc. Med.*, 36, 286).

This third group deserves our attention and careful investigation, expecially from the endocrinological point of view.

Dr. W. R. Trotter: I agree with Dr. Freudenthal that we are here dealing with three quite separate conditions which affect the skin. There is first generalized myxœdema—hypothyroidism. Then pretibial myxœdema, which is invariably associated with a toxic goitre, although it may not appear until after the toxic goitre has been treated by thyroidectomy; nevertheless, it always appears in association with a toxic goitre. Finally there is the third group of which the present case is a good example. One would like to find some association with thyroid disease, but so far there is no direct evidence. Here, I think, we have to beware of falling into a terminological trap, for the term "myxœdema" is used in two quite separate senses, namely, the sense commonly used in general medicine for the clinical picture produced by deficiency of thyroid secretion, and the literal sense in which it is used in dermatology for a mucinous infiltration of the skin. In this connexion I think the dermatologists have the right on their side, and if we could choose the sense in which the word is to be used it would be better if the term "myxœdema" were kept for use in its literal sense. However, I am afraid things have gone too far, and the term "myxœdema" is in such common use in the sense of hypothyroidism that there is no hope of recalling it. But as long as the term is used in two different senses there will continue to be a considerable amount of confusion. All we can say is that in Dr. Freudenthal's third group none of the cases has responded to oral thyroid extracts. That is certainly true of the pretibial type also, and they are unaffected by thyroidectomy. Only in the first group, associated with hypothyroidism, does the skin change at all when thyroid extract is administered. At the moment the third group remains a baffling and extremely interesting problem.

Dr. Freudenthal: Could the pituitary gland play a role in these conditions?

Dr. Trotter: All we can say in that connexion is that pituitary over-activity may occur and may be a common factor linking the cases of hypothyroidism and the cases of pretibial myxœdema and toxic goitre, but again I have nothing to say about the third group.

Dr. E. Lipman Cohen: The name "pretibial myxœdema" is becoming so firmly entrenched as descriptive of a group that it is liable to be misleading if it is taken too exclusively. Lesions have been found on the lower part of the abdomen and on the thighs. I have suggested the name "myxœdema circumscriptum thyrotoxicum".

Dr. Freudenthal: As long as so much uncertainty exists as to the pathogenesis of all three groups of myxœdema it may be best to keep this term and use it simply as a descriptive one. Or, we may try to introduce the term "mucinoses" to cover all conditions in which the presence of mucin is an esssential factor; it may include granuloma annulare (*Proc. R. Soc. Med.* 1945, 38, 333).

Sarcoidosis.—BERNARD GREEN, M.R.C.S., L.R.C.P., and C. W. F. MCKEAN, M.B.

Mrs. M. L., aged 41. Two children. In good general health. The eruption first commenced on her legs and forehead eight years ago. She now presents a striking appearance. On the forehead there are gyrate brownish lesions with a slightly elevated scaly edge, the centre being smooth and slightly atrophic. There are also several reddish-brown nodules on the face, and irregular infiltrating purplish and brownish plaques on the upper and lower limbs and shoulders. All the lesions are symptomless.

The eruption was not influenced during pregnancy.

Her brother died of pulmonary tuberculosis five years ago.

A biopsy was done and the section shows some granulomatous tissue in the dermis. The lesion consists of round aggregations of endothelial cells with an occasional foreign-body giant cell. There is no evidence of caseation, and the Ziehl-Neelsen film shows no tubercle bacilli to be present.

W.R. is negative. Mantoux test negative. E.S.R. 27 mm. in first hour (Westergren). A skiagram of the chest shows slight enlargement of the right upper mediastinal glands, but no pathological changes in the lungs. A skiagram of the bones of the hands reveals nothing abnormal.

Dr. Hugh Gordon: The lesions on this patient's face are similar to those of a patient of mine shown to the Section in January. She has two circular plaques on the right lower arm with raised edges and a scaly atrophied centre. The histology was that of a sarcoid. In this present case there are both these superficial scaly lesions with scarring present together with the more typical indurated lesions on the limbs.

Section of Laryngology

President—NORMAN PATTERSON, F.R.C.S.

[*March* 7, 1947]

The Diagnosis and Treatment of Tumours of the Nasopharynx

By E. D. D. DAVIS

THE tumours of the nasopharynx are difficult and unsatisfactory to treat but fortunately they are comparatively rare. I have studied the notes of 34 of my patients and the literature of a large number of other cases with the object of establishing an earlier diagnosis and more successful treatment. The 34 cases were seen during the past twenty-five years and consisted of 19 cases of carcinoma, 4 lymphosarcomata or lymphomata, 10 angiofibromata, 1 myxosarcoma of doubtful origin.

These are the types of tumours recorded by other observers but some call the fibroma or angiofibroma a fibrosarcoma. Two of the above angiofibromata turned out to be sarcomata and recurred some time after removal. This list does not include rare tumours such as ameloblastomas or adamantinomas which extend from the pituitary body along the craniopharyngeal canal or from the maxillæ into the nasopharynx. It is important to be able to recognize the degree of malignancy and the probable reaction to radiotherapy but at the present time there is considerable confusion in the nomenclature of various malignant and benign growths particularly carcinomata. The early diagnosis of these tumours is delayed because they are hidden in a cavity which is sometimes difficult to inspect. This inspection of the nasopharynx in patients who cannot tolerate the small mirror placed behind the soft palate is difficult and also in advanced cases of carcinoma when inability to open the mouth and fixation of the mandible is a symptom. Moreover a patient does not consult a doctor until the growth is large enough to produce a series of mechanical symptoms which are slow and insidious in onset and when it is frequently too late for successful treatment. Malignant growths within themselves do not produce any specific diagnostic symptoms or signs, and the general signs such as blood changes, cachexia, &c., are of no practical value in the early diagnosis. Gordon New of the Mayo Clinic reported 79 cases of malignant growths of the nasopharynx; 34 were epitheliomata and 33 were lymphosarcomata. It is interesting to note that of these 79 patients 74 had had an operation for the relief of symptoms without recognition of the fact that a primary growth in the nasopharynx was the cause of these symptoms. In 24 patients tonsils and adenoids

Differential blood-count: Leucocytes 6,900 (polys. 69%, lymphos. 26%, monos. 2%, eosinos. 3%).

The diagnosis became more uncertain, and the condition resembled chronic bullous pemphigus, but in September 1946 there was a much greater extension, the whole of the back, and to a less extent the chest, being covered with mixed, crusted hyperkeratotic and pigmented areas, with scattered bullæ and crusted impetigo-like lesions.

In January 1947 the face became involved, the whole area being covered with lupus erythematosus-like patches with seborrhœa of the scalp and the same general eruption on the trunk, only more acute. The distal parts of the extremities have never been affected to any great extent.

She was admitted to the Royal Sussex County Hospital in February, and treated by intramuscular penicillin, 30,000 units, three-hourly, for over 5,000,000 units, and during this period there was a great improvement. She was also given three small transfusions of fresh, whole blood at weekly intervals, and there is no doubt that this has checked further outbreaks up to the time of showing her.

At the time of her discharge her white blood-count read: Polys. 51%, lymphos. 39%, eosinos. 4%, monos. 6%.

On examination.—A healthy-looking woman. Partial dentures, teeth in good condition.

At present her face is practically clear, one small, pigmented scar on the forehead remains, but the trunk areas still show a rather complex picture of seborrhœa, pemphigus-like scars, and erythematoides.

POSTSCRIPT (4.10.47).—Since showing this case the patient has had an acute exacerbation, and antrypol has proved valueless.—E. C. J.

Dr. P. J. Feeny: One might possibly settle the diagnosis in this case as to whether it is pemphigus or not by giving antrypol. Dr. Burrows and I have had about 10 cases in children, mostly in Romford, during the past few years, and practically every one of them has been cured by antrypol. Included in this series were cases of "bullous eruption" such as one I showed here on November 16, 1944 (*Proc. R. Soc. Med.*, 38, 143, 1945) where the diagnosis of pemphigus is not universally agreed. Another B.P. Suramin (the German drug "Germanin") had no effect whatever. The dose of antrypol we used was 0·125 gramme intravenously or intramuscularly once a week for ten weeks and further similar courses when necessary after a two months' rest. In adults we have had considerable success on the same lines, using a dose of 0·25 gramme. In elderly people we have had no success at all.

Dr. Colin Jones: My experience with suramin and germanin is not quite so good. Recently I have had two cases of pemphigus treated with germanin without any response at all. We happened to have some of it in stock dating from pre-war days.

Dr. Brian Russell: I have recently had unfavourable results in the treatment of two cases of pemphigus with antrypol brand of suramin (B.P.) and am not convinced of its value in this disease. The occurrence of spontaneous remissions with pemphigus must also be kept in mind, in assessing results.

Recently I saw a patient clinically resembling pemphigus vegetans in a very severe form who reacted well to sulphapyridine but relapsed on its withdrawal, so presumably must be regarded as suffering from dermatitis herpetiformis.

Dr. W. N. Goldsmith: There is much confusion between the names Antrypol, Germanin, and Suramin.

Germanin (Bayer 205) first became a subject of British interest in 1921 when an expedition carried out large-scale experiments in South Africa (*Trans. R. Soc. trop. Med. Hyg.*, 1924, 17, 445, 464). After that, the Germans experimented with it, and in 1927 it became commercially available.

Antrypol has been made since 1933 by Imperial Chemical Industries, but was at first marketed for them by British Drug Houses. It is a brand of Suramin, a term which was introduced early in the war as an English equivalent of the foreign Germanin, and in 1941 was included in the 4th Addendum to the British Pharmacopœia, 1932. Suramin is the sodium salt of m-benzoyl-m-amino-p-methylbenzoyl-1-aminonaphthalene-4 : 6 : 8-trisulphonic acid.

The formula of Bayer 205 has not been given, but "there is every reason to suppose that it is identical with Suramin" (Davis).

NOTE (W. N. G).—The above remarks have, since the discussion, been corrected in accordance with information elicited from Mr. H. Davis, Ph.D., Chief Pharmacist at University College Hospital.

The superficial lymphatic glands along the posterior border of the sternomastoid are involved early. Gordon New has recorded two cases of paralysis of the nerves in the jugular foramen. A persistent sore throat is said to be an early symptom.

Nasal symptoms especially epistaxis or a blood-stained mucous discharge from the nasopharynx accompanied by headache in a patient of cancer age is suspicious, and a careful examination of the nasopharynx with the post-nasal mirror, the endoscope passed through both nostrils alternately, and with the finger, should be made. Good illumination and a direct view of the nasopharynx can be obtained by retracting the palate with a special Coolite retractor or curved pencil torch. The nasopharynx thus illuminated can be clearly seen when looking through the anterior nares with a large nasal speculum.

Beck of Chicago has devised an ingenious method of retracting the palate by passing a small bore rubber catheter through both nostrils and bringing the ends out through the mouth and applying forward and upward traction. These methods of *examination* of the nasopharynx are essential to the early diagnosis of new growths of this area. An X-ray photograph which shows the extent of the growth is useful. Nasal obstruction except in cases of angiofibroma is not common. When the growth is accessible, and it is practical, as large a piece as possible should be removed for microscopy to clinch the diagnosis and for radiotherapy. A biopsy of a nasopharyngeal fibroma is inadvisable for reasons given below. Sometimes a lymphatic gland with metastasis is available and is more useful for a biopsy than a piece removed from the nasopharynx.

The treatment of malignant growths of the nasopharynx is confined to deep X-ray therapy. These cases are inoperable and beyond surgery when first seen. Deep X-ray therapy is more hopeful now that an earlier diagnosis is made and the technique has improved. All the 19 cases mentioned above derived little benefit from radium or deep X-ray therapy and all of them died within twelve to eighteen months from the first appearance of the symptoms. Radium was most unsatisfactory because it caused considerable reaction with pain and irritation of the mucosa and was followed by metastases. The lymphosarcomata and the lympho-epitheliomata disappeared rapidly with radium treatment but the cases all died of metastases within two years. However deep X-ray therapy is the only treatment which holds out any hope of success or even relief.

The bleeding fibroma of male puberty is benign and occurs in boys between the ages of 10 and 20. I have not seen a case in a girl, or a true fibroma after the age of 25. It is a sessile, globular, solid, hard, fixed tumour usually growing from the body of the sphenoid or from the inaccessible roof of the posterior nares. It bleeds freely when touched or spontaneously. Nasal obstruction is the first symptom followed by profuse epistaxis which is more often provoked than spontaneous. The tumour grows and extends within the nasal cavity and even into the nasal sinuses. It is said to disappear about the age of 25, but that has not been my experience, though growth and extension may be slower. I do not know of, nor can I find, the record of any case which has disappeared spontaneously. Nearly all the recorded cases have been treated by enucleation, excision by diathermy or by radiotherapy. The histology of the fibroma is typical and consists of dense fibrous tissue with numerous cavernous blood spaces and in some tumours these spaces are more numerous near the surface of the growth. The tumour is very vascular and for this reason it is frequently called an angiofibroma. A biopsy is unsatisfactory and misleading because it is difficult to remove a sufficiently large piece and only a section of the whole or greater part of the tumour is of real value. The removal of a small piece results in repeated and profuse epistaxis which demands prolonged packing. This is followed by sepsis and had been removed; in 18, glands in the neck; in 12, the wisdom or third molars had been extracted. Various intranasal operations had been performed in 19, and finally a mastoid operation for the relief of pain.

The symptoms and signs of carcinoma of the nasopharynx vary with the site and type of growth and the commonest site is the lateral wall. When the growth is in the region of the eustachian tube or lateral wall the first symptom may be a unilateral deafness with fluid in the middle ear as the result of eustachian obstruction. This is known as the auricular type of growth and it was the first symptom and sign in 3 of my 19 cases. Sometimes a diagnosis has not been made until secondary growths appear in the cervical lymphatic glands. *The glandular type* of case shows the enlargement of the deep cervical glands at the angle of the jaw on both sides of the neck or the superficial group of glands along the posterior border of the sternomastoid. This was the first sign in six cases. This is the type of case for which tonsils have been enucleated or a dissection operation for glands in the neck has been performed before the diagnosis of carcinoma of the nasopharynx has been made. The enlargement of the lymphatic glands is the first sign of a lympho-epithelioma or lymphosarcoma.

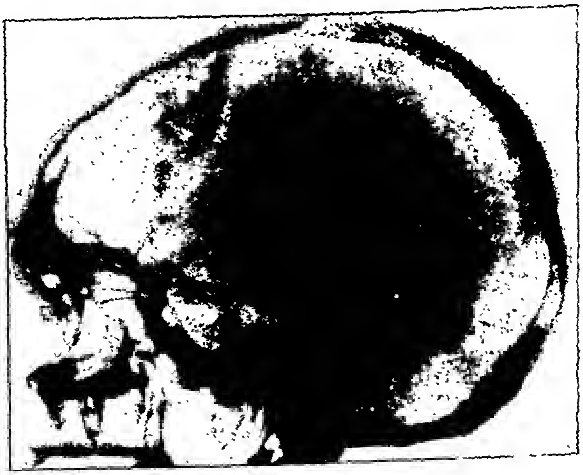


FIG 1.

Neurological symptoms such as headache, pain, diplopia and paralysis of cranial nerves were the first symptoms in six cases. These patients are seen first by the ophthalmic surgeon or neurologist and the primary nasopharyngeal lesion may escape detection. The *headache* is bitemporal or on the vertex of the skull. A *neuralgia of the fifth cranial* nerve or upper cervical spinal nerves is occasional but pain in the distribution of the auriculo-temporal nerve is more common. Paralysis of the sixth cranial nerve first on one side and then on both is commonest. It is followed by ptosis and paralysis of the third nerve and later a complete ophthalmoplegia on the one side and a partial on the other. Proptosis and displacement of the eyeball outwards is a later symptom and occurs when the tumour is very large. There is evidence to show that this growth may commence in the body or great wing of the sphenoid and later burrow to the surface in the nasopharynx particularly when a paralysis of a cranial nerve is the first sign and precedes the other symptoms by some weeks. Reproduced is an X-ray photograph of such a case showing erosion of the dorsum sellæ and body of the sphenoid. An infrasellar pituitary tumour may resemble a carcinoma of the nasopharynx but pituitary tumours more often produce a bitemporal hemianopsia, optic atrophy and other localizing signs.

In conclusion an attempt should always be made to enucleate the tumour, if that fails then Nélaton's operation should be undertaken, as described above to thoroughly expose the growth and completely to remove it by dissection and diathermy. If this is unsuccessful diathermy and radiotherapy can be tried.

REFERENCES

Drummond, W. A. D. (1939) *Proc. R. Soc. Med.*, 32, 200.
Eve, F. (1907) *Brit. med. J.* (i), 485.
Figi, F. A. (1940) *J. Amer. med. Ass.*, 115, 665.
Godtfredsen, E. (1947) *Proc. R. Soc. Med.*, 40, 131.
Milligan, W. (1924) *J. Laryng.*, 39, 537.
New, G. (1922) *J. Amer. med. Ass.*, 79, 10.
Shaheen, H. B. (1930) *J. Laryng.*, 45, 259.
Tilley, H. (1903) *J. Laryng.*, 18, 45.

A. J. Gardham said he first became interested in malignant nasopharyngeal tumours some twenty years ago. Even at that time they had been known for a considerable period. Perhaps the best clinical description of them was by Trotter in 1911, and they were quite well known in German literature long before that. He believed now that something like 2,000 cases were available for study in the literature. The reason why they were not more generally recognized was that they did not tend to go to one particular branch of the profession. In recent times they were usually sent to radiotherapists for treatment and they came almost equally from the various other branches, from laryngologists, ophthalmologists, neurologists, from general surgeons, and also from dentists.

The ophthalmological side of the picture had been dealt with recently in the Society, when it was emphasized that it was generally in late cases that the eye signs came into the picture (Godtfredsen, E., 1947, *Proc. R. Soc. Med*, 40, 131). The most common was a sixth nerve palsy followed in something like one-third of the cases by a third nerve palsy. The only other ophthalmological sign, a very late one, which was at all common was displacement of the eyeball. The appearance of ophthalmological signs in malignant tumours of the nasopharynx, meant that the tumour was very far advanced, and that prospects of success, even in palliative treatment, were poor. Paralysis of the third and sixth nerves generally indicated intracranial extension.

Intracranial extension ultimately happened in a fair proportion of cases, and was responsible for taking some of these patients primarily to a neurologist, but the majority which presented first to neurologists showed themselves as a fifth nerve neuralgia. Other cranial nerve palsies were seen in the late stages, and while many patients died of distant metastases, quite a proportion ultimately developed progressive paralysis of the various nerves round the jugular foramen and ended their days with something very like a bulbar palsy.

Those cases which came from general surgeons usually had to do primarily with the glands in the neck. Enlargement of these glands was a common initial symptom in his series. The glands were extremely puzzling to those who did not know about malignant nasopharyngeal tumours, particularly in cases arising in young adults. The glands had not the ordinary characteristics of carcinoma: they were much softer, commonly bilateral, and very easy to mistake for tubercle. The clinical difficulties were increased because cases showing enlargement of the glands of the neck as a first symptom were often in the same age-group as tubercle. Swelling in the temporal fossa was also an occasional early sign which brought patients under the notice of general surgeons.

Very often patients with malignant tumours of the nasopharynx were first seen by dentists because they had pain in the upper or lower jaw which was presumed to be due to bad teeth, and a considerable proportion were treated by dental extraction before they were ever seen by any branch of the medical profession.

Nowadays, he supposed, more of these tumours went to the radiotherapist than to anybody else. There was no doubt that radiotherapy was the treatment of choice; perhaps the only treatment except purely palliative measures, but the mechanism whereby patients came to the radiotherapist was not always satisfactory. They arrived there simply because they were suffering from obscure tumours in a difficult situation, and a good many of them arrived without any clear indication of the true nature of the disease.

He would not enter into the controversy about the microscopic characteristics of these growths. The picture, as he saw it, was that of an infiltrating tumour at the base of the skull, with a very strong tendency to spread submucously and subperiosteally without ulceration. This could often be seen in the microscopic section. As a result of this tendency there were often none of the symptoms associated with ulceration, but many, such as infiltration of the soft palate and swelling in the temporal fossa, which arose from submucous and subperiosteal spread. There was, characteristically, a quick reaction to radiotherapy, and a very strong tendency to recurrence, causing death either from local recurrence or from distant metastases within two or three years. He had seen tumours superficial sloughing. All suspicious nasopharyngeal tumours should be examined histologically after removal. The hard, solid, globular tumour seen and palpated in the nasopharynx of a young male subject renders the diagnosis of fibroma obvious. The true fibroma is benign and does not metastasize. There is no pain in spite of the fact that absorption of bone may occur. X-ray photographs should be taken to ascertain the extent of the growth. It is difficult to distinguish between a rapidly-growing fibroma and a fibrosarcoma. The fibrosarcoma is not so circumscribed. It is softer, more elastic, and spreads into the nasal sinuses and cranial cavity. The bridge of the nose is expanded and first one eye and then the other is proptosed and displaced outwards producing what is known as the "frog face". The surface of the growth in the nasopharynx ulcerates and bleeds readily. If a fibroma which has been completely removed recurs it is in all probability a sarcoma. The section shows larger blood spaces and many more round cells. A positive diagnosis cannot be made on the section alone. The choanal or post-nasal polyp arises from the middle meatus of the nose and, taking the line of least resistance, projects through the posterior nares or choana into the nasopharynx and is easily recognized. I have not seen an angioma or cavernous angioma of the nasopharynx; these are difficult to treat by surgery and should be untouched.

The ideal treatment of a fibroma is enucleation of the tumour but the difficulty of access with complete exposure of the tumour accompanied by severe hæmorrhage makes enucleation sometimes impossible and unsatisfactory. The lower edge of the tumour can be seen well if the Davis gag is used with full extension of the neck and the soft palate forcibly retracted. When the tumour is exposed the mucous membrane is incised by the diathermy needle as far round the lower pole of the tumour as possible. Then a strong, slightly curved, flat dissector can shell out the tumour, particularly if the line of cleavage is found. If the tumour is attached to the roof of the posterior nares a dissector or raspatory can be used through both the nostrils and the nasopharynx. The hæmorrhage though profuse is not so alarming as in the past because the patient is given an intratracheal anæsthetic, the pharynx is packed off and a suction pump is used freely. The hæmorrhage can always be controlled by firm packing through the nostrils and with a captive swab introduced behind the soft palate. A blood transfusion can be given at any moment. In my experience ligature of the external carotid or compression of both external carotids does not control the bleeding to any appreciable extent. Enucleation by snare is sometimes impracticable owing to the difficulty of surrounding the tumour with the loop of wire (Lack's method). If enucleation by an attack through the nasopharynx and the nostrils fails then a complete exposure of the tumour is desirable. The best exposure is obtained by Nélaton's operation in which a large window is made in the hard palate, but the soft palate should not be completely divided. If the soft palate is divided the contraction of its muscles produces a wide gap so that a satisfactory union by sutures cannot be obtained. Nélaton's operation gives a much more complete exposure and does less damage to the nose than Moore's lateral rhinotomy or trans-maxillo nasal operation or Eve's displacement of the maxilla or even Rouge's operation. The implantation of radium in my experience has no beneficial effect and does not diminish the hæmorrhage if the tumour has to be removed later, moreover the burning of the mucosa results in considerable misery and pain to the patient.

Figi, who reviewed the notes of 63 cases seen at the Mayo Clinic during a period of thirty years, favours diathermy coagulation followed by radium or deep X-ray therapy over a prolonged period of two or more years. 19 patients aged 21 to 25 were so treated with favourable results. He does not think the results were due to retrogression which, it is alleged, occurs about the age of 25. The accurate application of radium is difficult and Figi implanted radon seeds or radium. Radiotherapy is followed by atrophy of the mucosa. He does not favour enucleation or excision.

In conclusion an attempt should always be made to enucleate the tumour, if that fails then Nélaton's operation should be undertaken, as described above to thoroughly expose the growth and completely to remove it by dissection and diathermy. If this is unsuccessful diathermy and radiotherapy can be tried.

REFERENCES

Drummond, W. A. D. (1939) *Proc. R. Soc. Med.*, 32, 200.
Eve, F. (1907) *Brit. med. J.* (i), 485.
Figi, F. A. (1940) *J. Amer. med. Ass.*, 115, 665.
Godtfredsen, E. (1947) *Proc. R. Soc. Med.*, 40, 131.
Milligan, W. (1924) *J. Laryng.*, 39, 537.
New, G. (1922) *J. Amer. med. Ass.*, 79, 10.
Shaheen, H. B. (1930) *J. Laryng.*, 45, 259.
Tilley, H. (1903) *J. Laryng.*, 18, 45.

A. J. Gardham said he first became interested in malignant nasopharyngeal tumours some twenty years ago. Even at that time they had been known for a considerable period. Perhaps the best clinical description of them was by Trotter in 1911, and they were quite well known in German literature long before that. He believed now that something like 2,000 cases were available for study in the literature. The reason why they were not more generally recognized was that they did not tend to go to one particular branch of the profession. In recent times they were usually sent to radiotherapists for treatment and they came almost equally from the various other branches, from laryngologists, ophthalmologists, neurologists, from general surgeons, and also from dentists.

The ophthalmological side of the picture had been dealt with recently in the Society, when it was emphasized that it was generally in late cases that the eye signs came into the picture (Godtfredsen, E., 1947, *Proc. R. Soc. Med*, 40, 131). The most common was a sixth nerve palsy followed in something like one-third of the cases by a third nerve palsy. The only other ophthalmological sign, a very late one, which was at all common was displacement of the eyeball. The appearance of ophthalmological signs in malignant tumours of the nasopharynx, meant that the tumour was very far advanced, and that prospects of success, even in palliative treatment, were poor. Paralysis of the third and sixth nerves generally indicated intracranial extension.

Intracranial extension ultimately happened in a fair proportion of cases, and was responsible for taking some of these patients primarily to a neurologist, but the majority which presented first to neurologists showed themselves as a fifth nerve neuralgia. Other cranial nerve palsies were seen in the late stages, and while many patients died of distant metastases, quite a proportion ultimately developed progressive paralysis of the various nerves round the jugular foramen and ended their days with something very like a bulbar palsy.

Those cases which came from general surgeons usually had to do primarily with the glands in the neck. Enlargement of these glands was a common initial symptom in his series. The glands were extremely puzzling to those who did not know about malignant nasopharyngeal tumours, particularly in cases arising in young adults. The glands had not the ordinary characteristics of carcinoma: they were much softer, commonly bilateral, and very easy to mistake for tubercle. The clinical difficulties were increased because cases showing enlargement of the glands of the neck as a first symptom were often in the same age-group as tubercle. Swelling in the temporal fossa was also an occasional early sign which brought patients under the notice of general surgeons.

Very often patients with malignant tumours of the nasopharynx were first seen by dentists because they had pain in the upper or lower jaw which was presumed to be due to bad teeth, and a considerable proportion were treated by dental extraction before they were ever seen by any branch of the medical profession.

Nowadays, he supposed, more of these tumours went to the radiotherapist than to anybody else. There was no doubt that radiotherapy was the treatment of choice; perhaps the only treatment except purely palliative measures, but the mechanism whereby patients came to the radiotherapist was not always satisfactory. They arrived there simply because they were suffering from obscure tumours in a difficult situation, and a good many of them arrived without any clear indication of the true nature of the disease.

He would not enter into the controversy about the microscopic characteristics of these growths. The picture, as he saw it, was that of an infiltrating tumour at the base of the skull, with a very strong tendency to spread submucously and subperiosteally without ulceration. This could often be seen in the microscopic section. As a result of this tendency there were often none of the symptoms associated with ulceration, but many, such as infiltration of the soft palate and swelling in the temporal fossa, which arose from submucous and subperiosteal spread. There was, characteristically, a quick reaction to radiotherapy, and a very strong tendency to recurrence, causing death either from local recurrence or from distant metastases within two or three years. He had seen tumours superficial sloughing. All suspicious nasopharyngeal tumours should be examined histologically after removal. The hard, solid, globular tumour seen and palpated in the nasopharynx of a young male subject renders the diagnosis of fibroma obvious. The true fibroma is benign and does not metastasize. There is no pain in spite of the fact that absorption of bone may occur. X-ray photographs should be taken to ascertain the extent of the growth. It is difficult to distinguish between a rapidly-growing fibroma and a fibrosarcoma. The fibrosarcoma is not so circumscribed. It is softer, more elastic, and spreads into the nasal sinuses and cranial cavity. The bridge of the nose is expanded and first one eye and then the other is proptosed and displaced outwards producing what is known as the "frog face". The surface of the growth in the nasopharynx ulcerates and bleeds readily. If a fibroma which has been completely removed recurs it is in all probability a sarcoma. The section shows larger blood spaces and many more round cells. A positive diagnosis cannot be made on the section alone. The choanal or post-nasal polyp arises from the middle meatus of the nose and, taking the line of least resistance, projects through the posterior nares or choana into the nasopharynx and is easily recognized. I have not seen an angioma or cavernous angioma of the nasopharynx; these are difficult to treat by surgery and should be untouched.

The ideal treatment of a fibroma is enucleation of the tumour but the difficulty of access with complete exposure of the tumour accompanied by severe hæmorrhage makes enucleation sometimes impossible and unsatisfactory. The lower edge of the tumour can be seen well if the Davis gag is used with full extension of the neck and the soft palate forcibly retracted. When the tumour is exposed the mucous membrane is incised by the diathermy needle as far round the lower pole of the tumour as possible. Then a strong, slightly curved, flat dissector can shell out the tumour, particularly if the line of cleavage is found. If the tumour is attached to the roof of the posterior nares a dissector or raspatory can be used through both the nostrils and the nasopharynx. The hæmorrhage though profuse is not so alarming as in the past because the patient is given an intratracheal anæsthetic, the pharynx is packed off and a suction pump is used freely. The hæmorrhage can always be controlled by firm packing through the nostrils and with a captive swab introduced behind the soft palate. A blood transfusion can be given at any moment. In my experience ligature of the external carotid or compression of both external carotids does not control the bleeding to any appreciable extent. Enucleation by snare is sometimes impracticable owing to the difficulty of surrounding the tumour with the loop of wire (Lack's method). If enucleation by an attack through the nasopharynx and the nostrils fails then a complete exposure of the tumour is desirable. The best exposure is obtained by Nélaton's operation in which a large window is made in the hard palate, but the soft palate should not be completely divided. If the soft palate is divided the contraction of its muscles produces a wide gap so that a satisfactory union by sutures cannot be obtained. Nélaton's operation gives a much more complete exposure and does less damage to the nose than Moore's lateral rhinotomy or trans-maxillo nasal operation or Eve's displacement of the maxilla or even Rouge's operation. The implantation of radium in my experience has no beneficial effect and does not diminish the hæmorrhage if the tumour has to be removed later, moreover the burning of the mucosa results in considerable misery and pain to the patient.

Figi, who reviewed the notes of 63 cases seen at the Mayo Clinic during a period of thirty years, favours diathermy coagulation followed by radium or deep X-ray therapy over a prolonged period of two or more years. 19 patients aged 21 to 25 were so treated with favourable results. He does not think the results were due to retrogression which, it is alleged, occurs about the age of 25. The accurate application of radium is difficult and Figi implanted radon seeds or radium. Radiotherapy is followed by atrophy of the mucosa. He does not favour enucleation or excision.

Section of the History of Medicine

President—Sir ARTHUR MACNALTY, K.C.B., M.D.

[*May* 8, 1947]

The Pre-History of Midwifery. [*Abridged*]

By I. HARVEY FLACK, M.D.

SOME years ago I began to collect material for a history of midwifery. It soon became clear that, as in every branch of medical history, there are individuals, periods, and phases about which whole libraries have been written. There are as many other periods about which there is little or no information and surprisingly little speculation. The longest and, to my mind, one of the most interesting of these periods is that which stretches backwards from the time of Soranus into man's pre-history. During this period women were presumably having babies. The birth-process was presumably much the same as to-day but the customs associated with it must have developed according to some pattern. I have been speculating as to the nature of that pattern. So much of the material on which these speculations are based is taken from Ploss, Bartels, and Bartels (1935) that I have indicated in the text only the few other authorities consulted. It may be assumed, therefore, except in the few instances attributed to other workers, that every thread in this speculative pattern is contributed by either Ploss or the Bartels. For example, they quote the Dyak legend of how midwifery began. This was originally recorded by Howell in 1906:

Kelili Badak Resa, whose wife was called Teburi, went into the jungle. Teburi was big with the child of Kelili. Kelili moved without noise seeking what food there might be. He came at length to the place of the *maias*. Unseen by the big monkeys Kelili watched. He saw what he had not seen before. A young female with a great belly was calling out with pain. She crouched upon the ground and her husband waited beside her. Kelili waited, waited for long till the birth was over, and Kelili marvelled for he saw how the husbands among the *maias* helped their wives at the birth of their young. All this he remembered and when the birth pains came to Teburi he helped her, doing all that he had seen the *maias* doing.

That is the Dyak story of how midwifery began. Every present-day savage tribe has the same kind of story, but they differ greatly in detail in different parts of the world.

In the beginning, when women gave birth to children, they might or might not be helped. Whether they were helped by men or by women or not at all depended on the degree of social development of the community. In the most primitive communities the woman remained alone and helped herself if she could. Her menfolk would welcome the child, especially a boy, but were quite indifferent to the process of bringing him into the world. Intuition—for want of a better word—would lead the primitive woman, as it does animals, to bear her young and to sever with her teeth the umbilical cord. It is likely that her labour was fairly easy.

Later, and this represented a not unimportant cultural advance, the husband no longer forsook the woman in labour, but remained with her and helped her, very much as Kelili is said to have done. This is what happens with the natives of the Brazilian interior. As soon as the woman feels that birth is beginning she lies on the ground. The husband stays with her and when the child appears he ties the umbilical cord. The tied cord he then bites through, leaving the placenta to be delivered in the usual way. The child he paints with red and black pigments before laying it ceremoniously in a specially prepared cot. Among with similar characteristics involving the upper jaw, but attempts to correlate these characteristics with microscopic appearances had not met with much success.

There was another queer thing about malignant nasopharyngeal tumours, namely, their remarkable geographical distribution. The only knowledge he had of this was based on an article describing a large series of cases from Hong Kong, where they accounted for something like 25% of malignant surgical lesions. No explanation was offered of this fact, but there was no doubt that the cases were the same as those about which they were talking. Another point which was very important was the close relation between these tumours and sepsis; he did not know which came first. One obvious septic complication was blocking of the eustachian tube by the tumour, followed by suppuration of the middle ear. That was purely mechanical, but there were many cases in which the sequence of events was less obvious: A patient who was first seen about the middle of 1946 was diagnosed as having a retropharyngeal abscess, because of a swelling in the left side of the neck, increasing in size and causing difficulty in swallowing. There was a rather indefinite past history, which included nasal obstruction on the left side of many months' duration. The suppurating swelling in the neck was incised, and the patient got better, but not well. Six months later he was seen at the radiotherapy clinic at University College Hospital, and by that time it was quite obvious that he had a growth in the pharynx. It was a lympho-epithelioma of the nasopharynx. He was turned down for radiotherapeutic treatment on the grounds that the tumour was too advanced to justify it.

With a view to making the patient more comfortable he was treated for the sepsis in his nose and mouth associated with the tumour. He then had enlarged glands, was breathing with difficulty and appeared moribund. At his next visit, six months later, his stridor had disappeared, the growth was considerably smaller, and the vocal cords could just be seen. That was in February 1947, and in view of the very marked improvement, it was thought justifiable to treat him by radiotherapy. The patient had just reported again for re-examination on the previous day. He was subjectively better than he had been for years, the glands were much smaller, and he was breathing through his nose for the first time for over a year. Here was a case that might well have been turned down as completely untreatable, and to avoid making this mistake, it was necessary to recognize that in nasopharyngeal tumours, a considerable part of the symptoms and physical signs might be due to sepsis and not to the tumour itself.

Another instructive case was that of a man aged 21 whom he saw first in 1932, when the patient reported with painless lumps in the left side of the neck. He took a gland out for biopsy and the report came back as endothelioma. On examination there was found high up in the nasopharynx around one Eustachian orifice a little firm submucous swelling, and on the evidence of the previous biopsy, they believed that they were dealing with a case of endothelioma of the nasopharynx, as these malignant tumours were then called. In those days mass irradiation, deep X-rays, and teleradium, were not readily available, and, for want of a better method, he treated this man by the insertion of radon seeds around the region of his primary tumour, and carried out a bilateral resection of the glands of the neck. He last saw the patient three or four months ago, fifteen years after the original treatment; he had a recent discharging sinus in his neck, and breaking down glands in the posterior triangle. The condition was tuberculous all the time, and it illustrated the extraordinary difficulty of making a certain diagnosis in tumours affecting lymphoid tissue. Perhaps also it served to emphasize that a pathologist's report was not infallible.

The opportunity for surgical treatment, never great in the past, was now non-existent. Treatment was purely by irradiation. He had seen a fair number of the results of treatment by deep X-rays and teleradium, and they were very impressive, but it was important to realize that total eradication of the tumour was very unlikely. Disappearance of signs and symptoms for periods of two or even three years was often achieved, but ultimate recurrence was the rule, and there was nothing to suggest that alterations in the technique of local treatment could affect this outlook. Cases with signs of intracranial involvement (third and sixth nerve palsies) with increased intracranial tension were probably better left alone.

Short-term palliative treatment was usually of little avail. Mr. Gardham had, in his time, seen cases where neuralgia of the fifth nerve had been the predominant symptom, and he had tried to relieve them by injecting the gasserian ganglion, but his results had been 100% failures.

About half of these cases died with local extensions and the other half with distant metastases which often appeared in a very widespread field, and although sometimes the accessible ones were treatable, it generally meant that the patient was going to die in the course of the next six months.

As to their knowledge of midwifery, it must have been very meagre and dictated entirely by experiences handed down by word of mouth. Certainly some of them practised thoroughly bad midwifery for some superstitious or other reason. Thus among the desert tribes of Algeria one of the functions of the midwife was to delay the birth of the child. As soon as the head appeared and the child was half out of the womb the midwife would seize it firmly and hold it in position for at least fifteen minutes. This meant that the unfortunate mother had an unhappy quarter of an hour but it also ensured that the child would benefit from the enlightening experience of being kept forcibly at that mystic threshold of existence half-way between being born and not being born.

Some midwives are known to have practised version in the case of a breech presentation, especially in the case of the Swahili who, in addition, exercised a reasonable cleanliness and refrained from unnecessary manipulation. They also removed all the pubic hairs of the mother just before labour. The hairs were singed off and never cut, which implies not a hygienic reason but a magical one. Demons who might obstruct the labour would tend to lurk in the pubic hairs and though demons could be burnt out they could not be cut out. Swahili midwives were paid by giving them some of the pregnant woman's garments.

In some primitive communities, however, the duties of the midwife would extend beyond the actual labour and into the puerperium. This was the case in Siam where the midwife would care for both mother and child during the period of sacrificial purification. The birth of the child was always followed by a month of penance for the mother. For thirty days, five days in the case of subsequent children, she had to stay in the same special room and expose her naked abdomen and back to the heat of a fire which was kept burning night and day the whole time.

Among most pre-literate peoples special tabus, particularly about touching the ground or seeing the sun, relate to a woman who is menstruating. Even greater restrictions apply to the woman who has just borne a child. The Bantu regard menstrual blood as dangerous and puerperal blood as worse. But the blood from a miscarriage, and especially a concealed miscarriage is bad enough to cause droughts or famines. Frazer (1922) describes how an Australian aborigine discovered that his wife had lain on his blanket while she was menstruating. He killed her and himself died of terror within a few days. Aboriginal women are forbidden to touch anything that a man might use during the time they are menstruating. At childbirth all the clothes and vessels they use must be burned. Among many peoples the child-bearing woman, as in Siam, was regarded as dangerous to everybody. So she was secluded in some special hut for two or three weeks after labour. In the island of Kadiak, off Alaska, a woman who has borne a child is for twenty days so unclean that even her food has to be handed to her on long sticks. At a varying period after the birth purification rites are undertaken by the medicine-man and then the woman may resume her proper place in the tribe, free again from all the tabus.

Chinese women, for much the same reasons are steamed by their midwives all through the delivery and given a decoction of roasted human hair to drink. If the delivery is very painful a mixture of the excrement of bats with wild laurel and birthwort is given washed down with half a glass of urine which must be from a boy 3 or 4 years old. After delivery the patient is given a dish of dried afterbirth to eat and must have a fire underneath her bed for three days. The Chinese midwife feels the pulse in the middle finger of a pregnant woman to determine if the hour of birth is near. For her labour the woman is placed in a sitting position on a low bed with her back against the wall. Her feet are raised slightly on two bricks. As soon as the head appears the midwife knows the sex of the child—because a boy's head is always turned downwards, a girl's head upwards. The cord is cut with a red-hot iron rod and carefully preserved. The midwife continues to look after the mother for a month, taking care that no four-eyed person shall see her because this stops the flow of milk. A four-eyed person is a pregnant woman or her husband (Morse, 1934).

This then is as much as we can ever know about the beginning of midwifery. The process of birth was repeatedly observed and the simple and obvious things were done to help the woman in labour. Knowledge of these things was handed down, and normal births proceeded normally. Abnormal births were due to demons and where the demons were exceptionally powerful the midwives might reluctantly be compelled to call in the *shaman*. The belief on which the *shaman* worked was quite simple and was shared by most primitive peoples. Labour was supposed to be a voluntary act on the part of the child which was anxious to escape from its confined quarters. If the child was slow then it would be coaxed by the promise of food. If that failed it was threatened with dire penalties. A logical advance from this point was to take the woman out into the open and get a horseman to appear to ride her down. The charging horse turned aside at the last moment but the whole manœuvre which was popular among the American Indians was intended to frighten the child and make it hurry up its own delivery. If that failed then the woman would be laid the Marquesas islanders on Nukahiva the husband severs the umbilical cord not by biting it but by means of a sharpened flint.

Indian women of the Caraya tribe, who have settlements on the Rio Araguya in Brazil, are delivered in the squatting position. The woman squats on her heels and grasps a post with her hands. The husband takes up the same position immediately behind her and with both hands presses down on the contracting womb. Much the same assistance is given by husbands to the women of Gorngay and Tungu on the Malayan islands of Kola and Kobroor, while among the Unmatjera, an aboriginal tribe of North Australia, the husband's duties begin as soon as he knows his wife is pregnant. He rubs grease into the skin of her abdomen and sings a ritual song which is intended to make the child big and strong.

Among the natives of the Sandwich Islands assistance is given by an old man rather than by the husband. The woman is delivered sitting on his lap, and this always takes place in public.

In a later phase of development the husband was not actively engaged in assisting at the labour but had a symbolic role to play. In Guiana and among certain Caribbean tribes the husband takes to his bed and groans terribly to inform everyone of the pain he is sharing. Marco Polo observed the same custom in China six hundred years ago.

The next stage of cultural development excludes the husband completely and regards parturition as an exclusively female concern. Not so much from modesty as we know it but for mixed magical and social reasons birth is a purely feminine business and a thing to be kept from profane male eyes. Almost always assistance is given by older women who have themselves experienced childbirth. In certain groups, especially the Maori, there is a strict order of precedence. Assistance must be given by the maternal grandmother, or if she no longer exists, then the paternal grandmother presides. Failing her, the mother-in-law comes next.

Among the Trobriand Islanders, whose society is matrilineal and patrilocal, the pregnant woman goes to her father's house for there she can be looked after by her mother and her mother's kinsmen. All the males leave the house but keep guard outside to prevent the approach of sorcerers. The husband helps in this duty but plays a very minor part.

Malinowski (1929) was never allowed to witness a labour but he was fairly fully informed about it by the men and women he studied for so long. When the first pains are felt the woman is made to squat on a raised bedstead with a small fire burning under it. The fire is "to make her blood liquid" and it probably helps to keep away evil spirits.

For the actual delivery the woman is seated on a mat on the ground. Her legs are apart and her knees raised and she leans back resting on her hands. Immediately behind stands a sister or other close maternal relative. She presses down on the woman's shoulders "so that the baby may fall out quickly". The mother of the woman receives the child but no attempt is made to assist its delivery. If labour is prolonged or difficult then there are charms and words to counteract the evil magic that is obviously responsible.

Only in the most difficult cases, according to Malinowski, "would the child be manipulated and even then, from what I gathered, very timidly and incompetently". For example, if there was delay in the delivery of the afterbirth, a stone would be tied to the umbilical cord, but no attempt was ever made at manual removal. The first month of the puerperium both mother and child spend in the house and again on a bedstead beneath which a small fire is kept burning. No men are allowed in the house during this period but the husband may approach the door and talk to his wife without actually entering.

Another step forward is taken when the women of the family give way to "experienced women" and these must be regarded as the forerunners of the first midwives. Formal payment of these "wise women" was a later development but it has always been customary among the wives of Borneo head-hunters to give them presents of some kind as a reward for their assistance. Among the Sudanese, the Abyssinians, the Bedouins, and the Kabyle, "experienced women" are always present at a birth and usually arrangements are made well beforehand for their attendance. The wives of Hottentots and Bushmen order their "wise women" well in advance and are delivered lying on the left side. Three or four women sit round the woman in labour and take it in turn to exert pressure on the uterus at each pain.

From "experienced women" to the first midwives proper is another long step and it is not unreasonable to assume that this step has been taken when we find a tribe has a special word for these women and one that connotes something much more than "experienced woman." On the Tenimber and Timor Laut islands *wata sitong* is the word, on the island of Ceram *ahinatukaan*, in Fiji *alewa vuku*, in the Philippines *mabutin gilot*, and among the Basutos *babele xisi*. It is the fact, too, that these more than experienced women were not only called in for the actual birth but might be consulted in early pregnancy, even though such consultation was almost invariably for an opinion as to the sex of the unborn child.

As to their knowledge of midwifery, it must have been very meagre and dictated entirely by experiences handed down by word of mouth. Certainly some of them practised thoroughly bad midwifery for some superstitious or other reason. Thus among the desert tribes of Algeria one of the functions of the midwife was to delay the birth of the child. As soon as the head appeared and the child was half out of the womb the midwife would seize it firmly and hold it in position for at least fifteen minutes. This meant that the unfortunate mother had an unhappy quarter of an hour but it also ensured that the child would benefit from the enlightening experience of being kept forcibly at that mystic threshold of existence half-way between being born and not being born.

Some midwives are known to have practised version in the case of a breech presentation, especially in the case of the Swahili who, in addition, exercised a reasonable cleanliness and refrained from unnecessary manipulation. They also removed all the pubic hairs of the mother just before labour. The hairs were singed off and never cut, which implies not a hygienic reason but a magical one. Demons who might obstruct the labour would tend to lurk in the pubic hairs and though demons could be burnt out they could not be cut out. Swahili midwives were paid by giving them some of the pregnant woman's garments.

In some primitive communities, however, the duties of the midwife would extend beyond the actual labour and into the puerperium. This was the case in Siam where the midwife would care for both mother and child during the period of sacrificial purification. The birth of the child was always followed by a month of penance for the mother. For thirty days, five days in the case of subsequent children, she had to stay in the same special room and expose her naked abdomen and back to the heat of a fire which was kept burning night and day the whole time.

Among most pre-literate peoples special tabus, particularly about touching the ground or seeing the sun, relate to a woman who is menstruating. Even greater restrictions apply to the woman who has just borne a child. The Bantu regard menstrual blood as dangerous and puerperal blood as worse. But the blood from a miscarriage, and especially a concealed miscarriage is bad enough to cause droughts or famines. Frazer (1922) describes how an Australian aborigine discovered that his wife had lain on his blanket while she was menstruating. He killed her and himself died of terror within a few days. Aboriginal women are forbidden to touch anything that a man might use during the time they are menstruating. At childbirth all the clothes and vessels they use must be burned. Among many peoples the child-bearing woman, as in Siam, was regarded as dangerous to everybody. So she was secluded in some special hut for two or three weeks after labour. In the island of Kadiak, off Alaska, a woman who has borne a child is for twenty days so unclean that even her food has to be handed to her on long sticks. At a varying period after the birth purification rites are undertaken by the medicine-man and then the woman may resume her proper place in the tribe, free again from all the tabus.

Chinese women, for much the same reasons are steamed by their midwives all through the delivery and given a decoction of roasted human hair to drink. If the delivery is very painful a mixture of the excrement of bats with wild laurel and birthwort is given washed down with half a glass of urine which must be from a boy 3 or 4 years old. After delivery the patient is given a dish of dried afterbirth to eat and must have a fire underneath her bed for three days. The Chinese midwife feels the pulse in the middle finger of a pregnant woman to determine if the hour of birth is near. For her labour the woman is placed in a sitting position on a low bed with her back against the wall. Her feet are raised slightly on two bricks. As soon as the head appears the midwife knows the sex of the child—because a boy's head is always turned downwards, a girl's head upwards. The cord is cut with a red-hot iron rod and carefully preserved. The midwife continues to look after the mother for a month, taking care that no four-eyed person shall see her because this stops the flow of milk. A four-eyed person is a pregnant woman or her husband (Morse, 1934).

This then is as much as we can ever know about the beginning of midwifery. The process of birth was repeatedly observed and the simple and obvious things were done to help the woman in labour. Knowledge of these things was handed down, and normal births proceeded normally. Abnormal births were due to demons and where the demons were exceptionally powerful the midwives might reluctantly be compelled to call in the *shaman*. The belief on which the *shaman* worked was quite simple and was shared by most primitive peoples. Labour was supposed to be a voluntary act on the part of the child which was anxious to escape from its confined quarters. If the child was slow then it would be coaxed by the promise of food. If that failed it was threatened with dire penalties. A logical advance from this point was to take the woman out into the open and get a horseman to appear to ride her down. The charging horse turned aside at the last moment but the whole manœuvre which was popular among the American Indians was intended to frighten the child and make it hurry up its own delivery. If that failed then the woman would be laid the Marquesas islanders on Nukahiva the husband severs the umbilical cord not by biting it but by means of a sharpened flint.

Indian women of the Caraya tribe, who have settlements on the Rio Araguya in Brazil, are delivered in the squatting position. The woman squats on her heels and grasps a post with her hands. The husband takes up the same position immediately behind her and with both hands presses down on the contracting womb. Much the same assistance is given by husbands to the women of Gorngay and Tungu on the Malayan islands of Kola and Kobroor, while among the Unmatjera, an aboriginal tribe of North Australia, the husband's duties begin as soon as he knows his wife is pregnant. He rubs grease into the skin of her abdomen and sings a ritual song which is intended to make the child big and strong.

Among the natives of the Sandwich Islands assistance is given by an old man rather than by the husband. The woman is delivered sitting on his lap, and this always takes place in public.

In a later phase of development the husband was not actively engaged in assisting at the labour but had a symbolic role to play. In Guiana and among certain Caribbean tribes the husband takes to his bed and groans terribly to inform everyone of the pain he is sharing. Marco Polo observed the same custom in China six hundred years ago.

The next stage of cultural development excludes the husband completely and regards parturition as an exclusively female concern. Not so much from modesty as we know it but for mixed magical and social reasons birth is a purely feminine business and a thing to be kept from profane male eyes. Almost always assistance is given by older women who have themselves experienced childbirth. In certain groups, especially the Maori, there is a strict order of precedence. Assistance must be given by the maternal grandmother, or if she no longer exists, then the paternal grandmother presides. Failing her, the mother-in-law comes next.

Among the Trobriand Islanders, whose society is matrilineal and patrilocal, the pregnant woman goes to her father's house for there she can be looked after by her mother and her mother's kinsmen. All the males leave the house but keep guard outside to prevent the approach of sorcerers. The husband helps in this duty but plays a very minor part.

Malinowski (1929) was never allowed to witness a labour but he was fairly fully informed about it by the men and women he studied for so long. When the first pains are felt the woman is made to squat on a raised bedstead with a small fire burning under it. The fire is "to make her blood liquid" and it probably helps to keep away evil spirits.

For the actual delivery the woman is seated on a mat on the ground. Her legs are apart and her knees raised and she leans back resting on her hands. Immediately behind stands a sister or other close maternal relative. She presses down on the woman's shoulders "so that the baby may fall out quickly". The mother of the woman receives the child but no attempt is made to assist its delivery. If labour is prolonged or difficult then there are charms and words to counteract the evil magic that is obviously responsible.

Only in the most difficult cases, according to Malinowski, "would the child be manipulated and even then, from what I gathered, very timidly and incompetently". For example, if there was delay in the delivery of the afterbirth, a stone would be tied to the umbilical cord, but no attempt was ever made at manual removal. The first month of the puerperium both mother and child spend in the house and again on a bedstead beneath which a small fire is kept burning. No men are allowed in the house during this period but the husband may approach the door and talk to his wife without actually entering.

Another step forward is taken when the women of the family give way to "experienced women" and these must be regarded as the forerunners of the first midwives. Formal payment of these "wise women" was a later development but it has always been customary among the wives of Borneo head-hunters to give them presents of some kind as a reward for their assistance. Among the Sudanese, the Abyssinians, the Bedouins, and the Kabyle, "experienced women" are always present at a birth and usually arrangements are made well beforehand for their attendance. The wives of Hottentots and Bushmen order their "wise women" well in advance and are delivered *lying* on the left side. Three or four women sit round the woman in labour and take it in turn to exert pressure on the uterus at each pain.

From "experienced women" to the first midwives proper is another long step and it is not unreasonable to assume that this step has been taken when we find a tribe has a special word for these women and one that connotes something much more than "experienced woman." On the Tenimber and Timor Laut islands *wata sitong* is the word, on the island of Ceram *ahinatukaan*, in Fiji *alewa vuku*, in the Philippines *mabutin gilot*, and among the Basutos *babele xisi*. It is the fact, too, that these more than experienced women were not only called in for the actual birth but might be consulted in early pregnancy, even though such consultation was almost invariably for an opinion as to the sex of the unborn child.

each case extending right across the abdomen and round the hips to end in a leaf-shaped area on each buttock. This scar must have been produced deliberately, possibly with a red-hot cautery, and may have been a brand indicating the slave status of these two girls. In all five mummies the pelvis is tilted forwards and its measurements correspond much more closely to those of the female ape than to those of European women, evidence perhaps that the changes in the female pelvis following the assumption of the upright posture were effected more slowly in the negroid races than in the women of the Mediterranean area.

A papyrus of about 2200 B.C. was discovered at Kahun and forms part of the Petrie collection. The text is fragmentary but lays down the rules for the diagnosis of pregnancy, stressing particularly the early vomiting of pregnancy and the condition of the breasts. The Ebers papyrus, written about 1560 B.C. (Bryan, 1930), gives the same rules much more fully. It also describes methods for accelerating the birth and methods for inducing abortion. How to determine the quality of the milk of a nursing mother is the subject of one brief section which goes on to discuss disorders of the female breasts. "If the milk be good it smells like the pollen of the VAH—grain; if the milk be bad it smells like the entrails of the Mehit fish." For treating a diseased breast there was a plaster of Calamine, Cow's Brain, and Wasp's Dung, which was to be applied for four days. There was also a magic formula addressed to the "Breast of Isis who in the City of Xebt bore the gods Su and Tefnut".

The vulva could be protected against the entry of disease by a douche of which Garlic and Horn-of-a-Cow were the main ingredients. If this failed and the vulva became inflamed the formula was changed to Bile-of-the-Cow, Cassia and Oil. If the condition grew worse a douche of Fresh Dates and Hog's Bile was the answer, and if in spite of everything pustules appeared in the vagina Fresh Dates in Ass's milk was needed.

A later part describes how the child's future may be foretold. If it cries *Ni* it will live. If it cries *Ba* it will die. It would also die if it "let a loud lamentation be heard", or if it "looks down its face", so that looking down in the mouth is not as recent an expression as might have been supposed.

A remedy to stop the crying of a child was:—

"Pod-of-the-Poppy-Plant
Fly-dirt-which-is-on-the-Wall.
Make into One, strain, and take for four days.
It acts at once!"

The Ebers papyrus also describes many of the diseases of women much more clearly than does the Kahun text and gives details of methods of treatment and prevention. Menstruation was regulated either by douches of Wonderfruit, Fennel, Honey and Sweet Beer or by douches of Garlic and Wine. The Dried Liver of a Swallow in Sour Milk would protect the virgin who anointed herself with it from leucorrhœa. A recipe "in order to cause that a woman should cease to conceive for 1 year, 2 years, or 3 years" included "tips of acacia" mixed with honey and applied to a piece of lint which was placed in the vagina (Himes, 1936). Dates, Onions, and the Fruit-of-the-Acanthus crushed with Honey and applied to the vulva would cause abortion. Strangely enough this is the only abortifacient mentioned. We do seem to have progressed in some directions.

There are, however, many methods of accelerating the birth of a child. "Peppermint: Let the woman apply it to her bare posterior," is the simplest, and was probably no less effective than any of the other treatments suggested. To correct a displaced womb The-Film-of-Dampness-which-is-found-on-the-Wood-of-Ships rubbed in Yeast-of-Fermented-Beer was taken by mouth.

The Brugsch papyrus of 1350 B.C. describes a number of contraceptive specifics and has a section—presuming the failure of the contraceptives—on the signs of pregnancy. The description of these signs is an expansion of those outlined in the Kahun papyrus seven hundred years earlier and the same signs in the same order and almost word for word reappear a thousand years later in the Hippocratic writings.

From these and other papyri, particularly the Gardiner papyrus, which is mainly gynæcological, it is known that girls were usually married at the age of from 12 to 14 years. Even younger girls were used to strengthen the failing powers of enfeebled patriarchs. At an advanced age Mohammed selected two more wives aged 7 and 8 respectively, to help restore his health. The belief that young girls radiated vitality was shared alike by Mohammedans and Jews. The excision of girls was also practised extensively. This involves removal with a sharp knife of the clitoris and most of the labia minora. Mohammed himself said "Circumcision is an ordinance for men and honourable in women" but he was merely approving what had been practised for hundreds of years. There is still in existence a plaque of about 163 B.C. which records the details of a legal suit to recover the costs of clitoridectomy.

on her back so that her swollen abdomen might be jumped on, or she might be suspended from a tree while the enthusiastic midwives pulled down heavily on a strap round her abdomen and the *shaman* cheered them on.

The Hos of West Africa call a magician to aid the woman at any specially difficult birth. He says solemnly that the child is bound in the womb and so cannot be delivered. All the women entreat him to loose the bond. After some time he allows himself to be persuaded. Then creepers are brought from the forest and used to tie the woman's hands and feet. The magician takes a knife, calls the woman's name, and cuts through the creeper saying "I cut through thy bonds and the child's bonds". This is straightforward imitative magic and the same line of thought prompts the rule in many parts of the world that a woman in labour should have no knots near her person. All the knots in her garments and shoes are undone and all the locks in the house are solemnly unlocked.

In other pre-literate communities (Frazer, 1922) a rational approach may be combined with the magical. Thus among the Dyaks of Borneo any wizard who has to deal with a hard labour brings an assistant. Inside the birth-hut the wizard tries the obvious manipulations and tuggings, often with some success. Outside the hut his apprentice imitates the mother. A large stone is fastened to his belly by a cloth. This represents the child in the womb and, following the directions shouted to him from inside the hut, he moves the make-believe baby about, imitating exactly what is supposed to be going on in the process of birth.

So it was that men who had been excluded from the birth-hut returned to it, and sometimes if they were shepherds or swineherds they might apply to the obstructed labour the knives they had used on their animals. Carving up the child in the mother's womb and extracting it piecemeal was almost certainly the first phase of operative midwifery. The first step in operative gynæcology was removal of the ovaries which was practised by Indian and Australian natives. Himes (1936) quotes an account describing how the tribes living on the banks of the Condamine River operated on selected women, who were then turned over to all the men of the tribe. These tribes are also known to have attempted Cæsarean section.

So much and no more can be seen in the tribal mirror. We never can know the degree of distortion of that mirror. All we can do is to jump nearly a quarter of a million years and take up the earliest known writings of man. People who can write and record their customs are at an advanced stage of civilization, and there must be just as great an advance in their practice of obstetrics. The transition must have been long and probably slow, but its exact phases we can only guess at, remembering the enormous gulf that separates the unlettered savage from the priests and law-givers who committed to stone tablets and to papyri their laws and their customs.

Yet the savage and the lawgiver are descended from a common stock and the gulf between them is crossed over and over again by threads which show their unity. This is especially true of the customs relating to pregnancy and parturition.

In recent years obstetricians have been stressing the importance of posture in labour. Primitive women knew all about posture as an aid to easy delivery and automatically assumed the sitting, squatting, or kneeling position. Elaborations of these positions were the setting up of posts or crossbars to which the woman could cling. Only in civilized communities, and particularly after the discovery of anæsthesia, were women delivered in the recumbent position, which abandons one powerful factor in promoting the expulsion of the child, the pressure of the thighs on the abdomen. Now we are tending to return to the primitive postures because they were obstetrically effective (Jarcho, 1934).

Be it noted then as we turn from the mirror of tribal obstetric practice to the oldest written records we have that folklore is all of a piece the world over. If we find that Cleopatra's midwives were not very different from Queen Victoria's there is no need to attribute special prescience to the former or incredible conservatism to the latter. They were all women and they were handling the same problem. The process of birth has not changed, nor have the fears and joys to which it gives rise. But the customs surrounding it have become more specialized with the passing of time.

A careful study has been made by Derry (1935) of the bodies of five women of the 11th Dynasty, bodies that showed how well the *Taricheutae* had done their work. Menuhotep II reigned about 2050 B.C. The mummies are of five Nubian women who belonged to his harem. Two of them, Ashait and Henheit, must have died at the age of 22 or 23 years. The mummy of Henheit is so well preserved that it was possible to say why she died at this early age. She died as a result of a difficult labour which had torn both the vagina and the bladder so that a tear in the bladder communicated directly with the vagina. Two other mummies are of dancing girls and show extensive tattooing of the arms, legs, and feet, and of the lower abdomen just above the pubis. In addition there is a peculiar scar in palate. There is also a reference to an abnormally long pregnancy of 11/12 months, which implies that 9 months was known to be the usual duration of pregnancy. Of normal births there is no record except a mention of the assistance given by a midwife who was designated "knower of the inside". Demons abounded in Babylon and might be good or bad. Ishtar was an essential demon and without her help the fœtus would die before delivery. Labartu was another female demon but of a different complexion and given to tearing children prematurely from the mother's womb, and to carrying a child-bed fever which often proved fatal. Suckling, either by the mother or by a wet nurse, was carried on for three years quite commonly and charms and amulets were used to promote this extraordinarily prolonged flow of milk. An interesting case described in one of the tablets is that of a wet nurse who had a cancer of the breast which caused her death.

Next to the Egyptian papyri in antiquity are the four Vedas of Brahma. Again these are Sacred Books but the author is not Thoth but Brahma and one book proceeded from each of his four mouths somewhere about 140 B.C. Later Brahma produced a second group of sacred books, the Upavedas, one of which is the Ayurveda, and this contains the oldest Hindu medical and surgical writings. The section we are most concerned with is the Charaka Ayurveda of 120 chapters, which was actually written in the second century A.D. Linked with it is the *Sushruta Samhita*, and though Sushruta was supposed to be the pupil of Charaka the *Samhita* clearly dates from about 600 B.C. The exact order of appearance of these works never can be known and it may well be that there was a version of the Charaka Ayurveda which preceded the Sushruta Ayurveda (Bhishagratna, 1907).

Leaving the legends on one side, these two works by Charaka and Sushruta reveal clearly the practice of the ancient Hindus in both obstetrics and gynæcology. Their knowledge of anatomy was very superficial although dissection was not forbidden. It was the technique of preparing a body for dissection that probably created some difficulties. The usual procedure was to leave the body for some days in a stream until it became putrid, then the skin was removed with a stiff brush and the parts examined. Even so there are some anatomical points of interest. In women there are "two canals, the roots of which are the uterus, and the *Dhamanee* vessels, which convey the menses. When they are wounded, barrenness is caused, and the menses cease". This seems to be one of the earliest references to the fallopian tubes.

Twenty-four diseases of the female organs of generation are described very sketchily. Typical examples quoted by McKay (1901) are:

Bandhyá: difficult menstruation. Rub the genitals and lower abdomen with oil and ghee, and keep the vagina distended by a roll of cloth.

Biplutá: continuing pain in the genital organs.

Pariplutá: severe pain during intercourse. A piece of cloth soaked in oil is to be kept in the vagina.

Prodokoh: excessive bleeding at the periods accompanied by fever, giddiness, fainting and thirst. Apply cold and astringent medicines; avoid venery; and live on cool simple food.

Patragani: when the infant dies, or abortion has taken place, with a great discharge of blood.

Palani: when a large man has connexion with a small and young female, he injures the parts and produces this disease.

Mahati: when the vagina is very large.

In dealing with a difficult labour the obstetrician "having cheered the woman up" was told to use the knife but "in such a way that he by no possibility cuts a living child with it; for if a child is injured, the physician may destroy both child and mother together". For a normal labour Sushruta directs that the patient should be delivered by four women, "stout-hearted and of ripe age, who shall trim their nails well". These were midwives and were quite distinct from the women surgeons of a race in Rajputana, the Bhils. Their surgery was of the most primitive kind and consisted for the most part of applying a red-hot iron to cauterize anything and everything of which the patient might complain.

The *Sushruta Samhita* has also an excellent chapter on infant hygiene and nutrition and in this the purgative effect of honey on the newborn infant (sugar diarrhœa) is noted. Surgery is referred to at length and it seems that Cæsarean section was undertaken fairly often. Yet despite this advanced attack on the problem of obstructed labour the cause of the obstruction was still believed to be a demon. The *Rigveda* has an exorcism for such a demon, and in this as in other Indian charms the name of the demon is not spoken, and the appropriate god is called on to help: "May Agni, the destroyer of Raksha, joining in this prayer, drive away the disease of evil name which dwells in thy womb and bowels".

The duration of pregnancy was known to be ten lunar months and there were many ceremonies to guarantee a normal issue and keep away demons which might be hunch-

Incidentally, as recently as 1945 I myself saw in Egypt a score of young women who had had this mutilating operation performed. This was not in the uncivilized reaches of the Western Desert but in the even more uncivilized slums of Cairo, the capital city. In these girls, and presumably the same has always applied, the operation appeared to have achieved its anatomical but not its physiological objective. In this instance even the custom has not altered very much in 3,000 years.

With the important part that sexuality played in the life of the women of Ancient Egypt, it is easy to understand the importance that was attached to the cosmetic care of the genitalia. These papyri contain innumerable prescriptions for pastes to be applied to the genitals and for fumigants, many of which were elaborately scented and perfumed. There were also a number of prescriptions for substances to be rubbed on to the male organ "for increasing the love of the wife for her husband". In some of the smaller chemist's shops in Cairo I have seen very similar medicaments rubbing anachronistic shoulders with sulphonamide tablets and penicillin lozenges.

The duration of pregnancy was known and in the seventeenth century B.C. Westcar papyrus instructions are given for calculating the expected date of delivery. It must be realized that to relate intercourse with pregnancy and determine the duration of pregnancy was a big step forward. Many primitive peoples know of no such relation. The Ingarda tribe in Australia believe that the child is a product of some food the mother has eaten. The Buduna tribe firmly believed that their women bore half-caste children because the white settlers had introduced bread made of white flour instead of the dark native bread. The women ate the white bread and therefore they had half-white children. Malinowski (1929) describes how the Trobriand islanders believe that pregnancy follows rupture of the hymen by whatever means and that intercourse is intended purely for pleasure and has nothing to do with procreation. Fatherhood is a social rather than a biological concept with most primitive groups. Other tribes believe that someone other than the socially recognized "father" sends an invisible spirit-baby to enter the woman. The sender in some tribes is called the child's *Wororu* and while the *Wororu* is often the father's brother it may even be his sister or some other female relative who wishes the spirit-baby on to his "wife".

This absence of knowledge of the exact part played by the male in conception is also shown by the contraceptive practices of certain pre-literate societies (Himes, 1936). One primitive group, the Dahomey in West Africa, use a particular root which is crushed and applied as a high intravaginal plug. The natives of the Kasai Basin in Central Africa plug the vagina either with a cloth or with chopped grass. In both these groups the contraceptive intention is clear and the practice is rational. Among many other pre-literate peoples, however, the intention is the same but the practice is irrational or magical. Isleta Indians in New Mexico obtained from the medicine man a specially treated buckskin belt. Worn continually this will ensure barrenness. Stepping three times over a recently buried corpse is believed by the Ait Sáddĕn of Morocco to prevent pregnancy. Drinking water which has been used to wash a dead person is equally effective. Eating the hoof-parings of a mule will render a woman as sterile as the mule. Or else the man should eat before intercourse the oviduct of a hen. If this has been tied into a knot pregnancy cannot possibly result. And of course almost every tribe has decoctions and potions to ensure infertility.

In most tribes normal labours were conducted entirely by women. The same custom applied in Egypt and is well shown in bas-reliefs of the Royal birth-rooms at Luxor and in other temples. One of the best known of these shows a queen of the 18th Dynasty. She is in labour on an obstetric chair and has four midwives in attendance. Another is a bas-relief at the Temple of Esneh which is believed to show the labour of Cleopatra. The queen is in a squatting position and is assisted by a group of five women, one of whom holds two ankhs or Tau-crosses, royal symbols of generation. The child is almost full-grown at delivery, another symbolic recording of royal power.

The Westcar papyrus mentions the special birth-chair. In its simplest form this consisted of two stones, one to support each buttock of the bearing-down woman. Wall pictures of lying-in rooms at Philae and at Dendrah show that it was the custom for women to have their labours in special houses, all of which were decorated with pictures of Isis, the birth-goddess, with little Horus in her lap. Sometimes the principal figure represented was the cat-headed Pacht, the god of parturition. In Isis were later merged all the other gods and goddesses connected with birth and with fertility, excepting only the one male god of fertility who is always depicted with an enormous phallus. The Westcar papyrus also contains the only reference in any of these papyri to the birth of triplets. The birth of twins was apparently fairly common.

Relatively little is known of Babylonian obstetrics. There are in existence a few tablets with cuneiform inscriptions which treat of congenital deformities such as hare-lip and cleft-maidenhead. Considering this wildly improbable explanation, which has been believed apparently for centuries, it seems clear that there must have lived in Judea at one time an erstwhile virgin sufficiently quick-witted to tell a good story and stick to it.

The biblical laws about menstruation are well known. The book of Leviticus contains the sternest mandates about the purifying of women after childbirth, about the hygiene of menstruation, the abomination of sexual perversion, and the prevention of contagious diseases, and notably of leprosy and gonorrhœa, if it was gonorrhœa. It is easy to interpret these laws as showing an advanced knowledge of public health and preventive medicine. This, however, seems to be a too rational and civilized interpretation of practices which were more likely to stem from irrational savage tabus. So far as we can follow primitive lines of thought the belief seems to have been that each man or woman had an inherent godliness which was at its best when intact. A flow of any kind from inside the body to the outer world—and this would include the lochia after parturition, menstrual fluids, and any genital discharge whether from the male or female organs—exposed the personal god to harm. The outer world was full of demons awaiting just such an opportunity and the harm that might result could easily affect other members of the community. Therefore a menstruating woman, a woman after childbirth, and a man or woman with "an issue" was tabu or "unclean" and to be avoided. The whole concept is animistic, which is not to say that continuing experience had not affected it, so that the periods of tabu were more exactly defined. The point to remember is that the prohibitions were tabus however exact the regulations that framed them.

Thus no explanation other than irrational tabu will fit the regulation that a woman who had given birth to a boy was unclean for seven times thirty-three days but a woman who had given birth to a girl was unclean for fourteen times sixty-six days. There is a basis of tabu and an overlay of Assyro-Babylonian numerology. The same numerologists laid it down that seventh days or multiples of seventh days were unlucky (*Dies Atra*), which may well account for the prohibition of all activity on the seventh day. Seven also recurs over and over again in connexion with men and women who have "an issue".

Jewish midwives, again like their Persian and Indian sisters, had goddesses to aid them. Ashtaroth who is mentioned in the Bible was also called Astarte and was known to the Babylonians and Assyrians as Ishtar. Pomegranates and doves as symbols of fertility were sacred to the Syrian Ishtar and the dove was regarded as a "bringer of children" which links Ishtar, the primordial mother goddess, with Mary to whom the Holy Ghost came in the form of a dove.

I began this far-reaching and inevitably incomplete survey by giving the legendary Dyak answer to the question: How did midwifery begin? Any other legend would have served as well. There is no hope now of finding anywhere Neolithic man and Neolithic woman in a state of nature, and only such a finding would give us the correct answer. The life of the most primitive tribes studied in recent times may approach more or less closely to the natural state, and a study of their obstetric habits is as near as we can get to the beginnings of midwifery.

Women must have been helped when their birth-pains came on from the earliest times, if only because their cries, whether exaggerated or not, awaken sympathy in even the most primitive peoples. Help by the husband, for want of the right primitive term, by other women in the same family, and later by experienced women, does seem to follow a progressive pattern, though here again we are just as likely to have got the pattern wrong as right. The change from the obvious crude mechanical assistance to experienced assistance is an appreciable advance, but the next step forward represents the difference between the Stone Age and the Iron Age, the change from the family of cave-dwellers to the organized communities of pastoral tribes. It is the change from *babele xisi* kneading a Basuto abdomen to the operative obstetrics of the priest-physicians of Egypt and India and Israel. Simple observation of the recurring natural processes of birth in women and in animals allowed the young savage woman to prepare for her own hour of need a simple procedure which would meet the normal contingencies. A rather wider formula for the actions needed to meet different circumstances would be known to the women who had seen many births and assisted many different women. That much we can follow fairly easily, but the next step is the important one and we know nothing about it. We know about *babele xisi* and about the priest physicians but we cannot know where one took over from the other. It may be that midwives became more experienced to the point at which knowledge began, knowledge of their own limitations. At that point they would seek help from the surgeons and physicians, the men concerned with the sufferings and the physical afflictions of mankind. That is a guess, but it will bear scrutiny. There were surgeons long before there were obstetricians, though there must have been midwives before there were surgeons. Whatever the backed, fingerless, doublemouthed, and so on. All these demons tried to contort the unborn child to their own fearful shapes. Other "sealing spirits" were the demons responsible for female sterility. Phantom pregnancy was due to a special demon called *Naigamesa.*

The signs of approaching delivery were known and included the sinking of the belly, a feeling of heaviness in the abdomen, frequent passing of water, and a mucous discharge from the genitals. To expedite parturition the abdomen was to be pounded while the woman was made to walk about. Amulets would help and so would sneezing powders. Then at the end of the phase of dilatation of the cervix the child's head would press down more heavily, causing the bladder to be irritable and increasing the frequency of the pains. At this stage the midwives were enjoined to put the woman to bed and they were not to press on her abdomen except when she was having pains. Pressing down between the pains was not only useless but might make the child deaf, dumb, or deformed. Finally when delivery was effected the umbilical cord was to be tied with thread eight fingers-breadths' from the navel. The other end of the thread was passed round the child's neck and the cord was cut above the ligature. The afterbirth was awaited and once that had been delivered the woman's genitals were anointed with a special unguent.

The midwives undertook the handling of most normal deliveries but in any case of doubt a doctor was consulted and in unusual difficulty he could call in a sort of obstetric specialist. A doctor was always needed for anything other than a vertex presentation. If both legs presented then the fœtus would be drawn down gently by traction on the legs. If only one leg appeared, the other must be sought. If the breech presented it was to be pushed back so that the legs could be pulled down. A transverse presentation should be manipulated till the child's head could be brought down first as in a normal delivery.

When manipulation failed and the presentation was "irremediable" the doctor must resort to the knife. The skull was to be cut first and removed piecemeal, then the child's body could be extracted with a special pair of forceps. If this was not possible the head should be cut off and delivered in one piece by grasping the eye-sockets or the mouth. If the shoulders were stuck fast in the birth passage the child's arms must be cut off. These directions in the Sushruta are detailed and provide for every possible contingency.

The doctor was of course a priest and he was also responsible for consecrating the child's nurse, and for some reason this was always done on a Monday. High-caste women were always delivered by the priest-physician even for normal labours and delivery took place in a special birth-house which they entered some time during the ninth month. After delivery both mother and child were washed. The mother's milk for the first few days was not considered fit to use. When the priest approved she could start feeding her child and at the end of forty days or so she was regarded as free from "the uncleanness attached to her during confinement".

This period of forty days applied also to the women of Ancient Persia and in their case sexual intercourse during this period was regarded as a crime deserving death. The four midwives which Indian women expected were increased to ten in Persia, five to superintend the cradle, one for the left shoulder, one at the right, one to support the mother's neck, one to hold her fast round the middle and one to receive the child and divide the umbilical cord.

The Persians believed that there was a female as well as a male seed. If the male seed was stronger a boy would result, if the female a girl. If the male and female seed were equally strong then the woman would have twins or triplets. The references to female seed suggest that by this was meant the menstrual blood of which part was used for conception and the remainder flowed back into the woman and was converted into milk.

The Talmud makes it obvious that the Jews too had skilled midwives who were held in high esteem. The Talmud represents the oral law of the Jewish people. The text of the work is called the *Mishna* and the commentaries on it are the *Gamara* which were compiled during the first five centuries A.D. These midwives, or *Femina Vivida,* all seem to have used special stools or labour chairs. They examined the genitals with their fingers and occasionally with the whole hand, though this was discouraged. For their most difficult cases they called in doctors who were always Rabbis. These Rabbis vivisected female animals and knew that the womb could be removed without necessarily causing death. As a development of this experimental work it is believed that they undertook embryotomy and attempted Cæsarean section in the living as well as immediately after the death of a pregnant woman. They also made careful vaginal examinations and observed and described the hymen. The virgins of Judea till quite recent years were distinguished by a mincing walk and the tinkling of tiny bells. They all wore a chain of these bells just below the knees, and the explanation given for their use is that they confine the lower limbs within certain limits and do not allow of any striding or running, which might "rupture" the maidenhead. Considering this wildly improbable explanation, which has been believed apparently for centuries, it seems clear that there must have lived in Judea at one time an erstwhile virgin sufficiently quick-witted to tell a good story and stick to it.

The biblical laws about menstruation are well known. The book of Leviticus contains the sternest mandates about the purifying of women after childbirth, about the hygiene of menstruation, the abomination of sexual perversion, and the prevention of contagious diseases, and notably of leprosy and gonorrhœa, if it was gonorrhœa. It is easy to interpret these laws as showing an advanced knowledge of public health and preventive medicine. This, however, seems to be a too rational and civilized interpretation of practices which were more likely to stem from irrational savage tabus. So far as we can follow primitive lines of thought the belief seems to have been that each man or woman had an inherent godliness which was at its best when intact. A flow of any kind from inside the body to the outer world—and this would include the lochia after parturition, menstrual fluids, and any genital discharge whether from the male or female organs—exposed the personal god to harm. The outer world was full of demons awaiting just such an opportunity and the harm that might result could easily affect other members of the community. Therefore a menstruating woman, a woman after childbirth, and a man or woman with "an issue" was tabu or "unclean" and to be avoided. The whole concept is animistic, which is not to say that continuing experience had not affected it, so that the periods of tabu were more exactly defined. The point to remember is that the prohibitions were tabus however exact the regulations that framed them.

Thus no explanation other than irrational tabu will fit the regulation that a woman who had given birth to a boy was unclean for seven times thirty-three days but a woman who had given birth to a girl was unclean for fourteen times sixty-six days. There is a basis of tabu and an overlay of Assyro-Babylonian numerology. The same numerologists laid it down that seventh days or multiples of seventh days were unlucky (*Dies Atra*), which may well account for the prohibition of all activity on the seventh day. Seven also recurs over and over again in connexion with men and women who have "an issue".

Jewish midwives, again like their Persian and Indian sisters, had goddesses to aid them. Ashtaroth who is mentioned in the Bible was also called Astarte and was known to the Babylonians and Assyrians as Ishtar. Pomegranates and doves as symbols of fertility were sacred to the Syrian Ishtar and the dove was regarded as a "bringer of children" which links Ishtar, the primordial mother goddess, with Mary to whom the Holy Ghost came in the form of a dove.

I began this far-reaching and inevitably incomplete survey by giving the legendary Dyak answer to the question: How did midwifery begin? Any other legend would have served as well. There is no hope now of finding anywhere Neolithic man and Neolithic woman in a state of nature, and only such a finding would give us the correct answer. The life of the most primitive tribes studied in recent times may approach more or less closely to the natural state, and a study of their obstetric habits is as near as we can get to the beginnings of midwifery.

Women must have been helped when their birth-pains came on from the earliest times, if only because their cries, whether exaggerated or not, awaken sympathy in even the most primitive peoples. Help by the husband, for want of the right primitive term, by other women in the same family, and later by experienced women, does seem to follow a progressive pattern, though here again we are just as likely to have got the pattern wrong as right. The change from the obvious crude mechanical assistance to experienced assistance is an appreciable advance, but the next step forward represents the difference between the Stone Age and the Iron Age, the change from the family of cave-dwellers to the organized communities of pastoral tribes. It is the change from *babele xisi* kneading a Basuto abdomen to the operative obstetrics of the priest-physicians of Egypt and India and Israel. Simple observation of the recurring natural processes of birth in women and in animals allowed the young savage woman to prepare for her own hour of need a simple procedure which would meet the normal contingencies. A rather wider formula for the actions needed to meet different circumstances would be known to the women who had seen many births and assisted many different women. That much we can follow fairly easily, but the next step is the important one and we know nothing about it. We know about *babele xisi* and about the priest physicians but we cannot know where one took over from the other. It may be that midwives became more experienced to the point at which knowledge began, knowledge of their own limitations. At that point they would seek help from the surgeons and physicians, the men concerned with the sufferings and the physical afflictions of mankind. That is a guess, but it will bear scrutiny. There were surgeons long before there were obstetricians, though there must have been midwives before there were surgeons. Whatever the course of development there are no clear records of it. Development there must have been, unless we are to assume that Sushruta sprang fully-equipped from the womb of the Great Mother, but how it all happened cannot be known. Increasing observation led to certain customs and even to legal prohibitions and elaborate ritual. Then birth ceased to be something observed by the unknowing and became a subject for study. The study advanced more rapidly when men who had a surgical background and a wider culture were called in by midwives not as a last resource but in any case which promised to be difficult. However the transition came about it is true to say that for thousands of years everything that was done in obstetrics was done either by the midwives or by the surgeons. The surgeons would be women only rarely, only indeed at those few high peaks of civilization when women were given greater freedom and could become poets, or philosophers, or even doctors. The first such peak of which we have any detailed knowledge was the civilization of ancient Greece and there the midwives were skilled and the physicians and the surgeons more advanced than any that had been known previously.

REFERENCES

BHISHAGRATNA, K. K. L. (1907) The Sushruta Samhitá, Calcutta.
BRYAN, CYRIL P. (1930) The Papyrus Ebers, London.
DERRY, D. E. (1935) *J. Obstet. Gynæc.*, 42, 490.
FRAZER, J. G. (1922) The Golden Bough. London.
GARRISON, F. H. (1929) History of Medicine. London.
HIMES, N. E. (1936) Medical History of Contraception. London.
JARCHO, J. (1934) Postures and Practices During Labor among Primitive Peoples. New York.
MALINOWSKI, B. (1929) Sexual Life of Savages. London.
MCKAY, W. J. S. (1901) History of Ancient Gynæcology. London.
MORSE, W. R. (1934) Chinese Medicine. New York.
PLOSS, H. H., BARTELS, M., and BARTELS, P. (1935) Woman. London.

Section of Odontology

President—Professor H. Stobie, F.R.C.S., L.D.S.E.

[*March* 24, 1947]

Three Cysts in the Same Mandible, Not of Dental Origin. ? Solitary Cysts or Osteitis Fibrosa.—George T. Hankey, O.B.E., T.D., M.R.C.S., L.D.S.Eng.

14.3.46: The patient, a boy aged 15½ years, first attended the London Hospital complaining of toothache.

Family history.—Father died recently of phthisis; mother and two brothers alive and fit.

Previous diseases.—At age of 2½ years he fell on front teeth and broke them; the teeth were extracted later. He had measles, pneumonia and diphtheria when aged 4, and was ill thirteen weeks. No other illnesses.

Treatment.—$\frac{5|}{6|}$ were extracted for advanced caries; no other treatment.

11.9.46. Six months later patient again attended the London Hospital.

Complaint.—Inflammation, pain, and swelling of gum in $\lceil 8$ region of one day's duration, accompanied by tenderness left side of the neck.

On examination.—Gum behind $\lceil 7$ swollen and inflamed; left submaxillary glands enlarged. Slight general toxæmia. Advanced caries of $\frac{|6}{|7}$; $\frac{5|}{6|}$ missing; extracted six months earlier. General condition of the other teeth, good; a well-formed dentition had erupted normally.

Fig. 1.—X-ray of left lateral jaw—Irregular cystic area lying below roots of $\lceil 567$, with greatest thinning of bone below $\lceil 56$, similar to the appearance of a multilocular cyst or adamantinoma; but the youth of the patient was against this diagnosis. Advanced distal caries of $\lceil 7$ and mesial caries of $\lfloor 6$; $\frac{|8}{|8}$ unerupted, in normal position.

Immediate treatment.—Expectant, until acute inflammation subsided. Mouth cleaned up; penicillin lozenges by mouth.

course of development there are no clear records of it. Development there must have been, unless we are to assume that Sushruta sprang fully-equipped from the womb of the Great Mother, but how it all happened cannot be known. Increasing observation led to certain customs and even to legal prohibitions and elaborate ritual. Then birth ceased to be something observed by the unknowing and became a subject for study. The study advanced more rapidly when men who had a surgical background and a wider culture were called in by midwives not as a last resource but in any case which promised to be difficult. However the transition came about it is true to say that for thousands of years everything that was done in obstetrics was done either by the midwives or by the surgeons. The surgeons would be women only rarely, only indeed at those few high peaks of civilization when women were given greater freedom and could become poets, or philosophers, or even doctors. The first such peak of which we have any detailed knowledge was the civilization of ancient Greece and there the midwives were skilled and the physicians and the surgeons more advanced than any that had been known previously.

REFERENCES

BHISHAGRATNA, K. K. L. (1907) The Sushruta Samhitá, Calcutta.
BRYAN, CYRIL P. (1930) The Papyrus Ebers, London.
DERRY, D. E. (1935) *J. Obstet. Gynaec.*, 42, 490.
FRAZER, J. G. (1922) The Golden Bough. London.
GARRISON, F. H. (1929) History of Medicine. London.
HIMES, N. E. (1936) Medical History of Contraception. London.
JARCHO, J. (1934) Postures and Practices During Labor among Primitive Peoples. New York.
MALINOWSKI, B. (1929) Sexual Life of Savages. London.
MCKAY, W. J. S. (1901) History of Ancient Gynæcology. London.
MORSE, W. R. (1934) Chinese Medicine. New York.
PLOSS, H. H., BARTELS, M., and BARTELS, P. (1935) Woman. London.

Fig. 4.—Left lateral jaw, same as fig. 1, but six months after extraction of $\lvert\overline{567}$, and marsupialization of cyst cavity by removing outer wall. The cavity has been almost completely filled in with new bone.

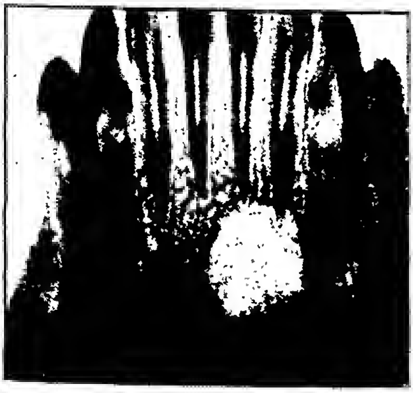


FIG. 3.

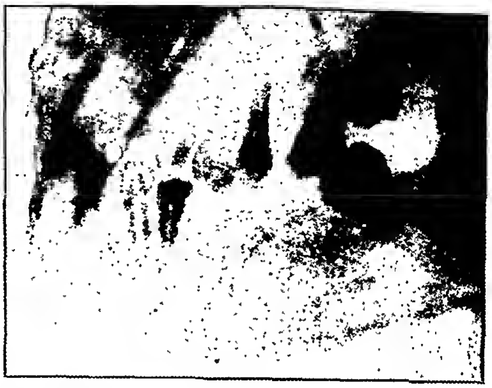


FIG. 4.

The points of interest in this case are:

Three cysts in the same mandible were only discovered through routine X-rays. An unusual X-ray appearance on one side always calls for a control view of the other.

The cysts were completely symptomless.

All the long bones were normal radiographically; the blood calcium and phosphorus were normal, thus excluding parathyroid disease. 14.4.47: X-rays taken of the skull, facial bones and teeth all showed normal structure.

The three cysts are situated in the regions of the marrow cavity present in young persons but later usually obliterated.

The cavity in the left body was unconnected with the teeth and the X-rays suggest that neither are the other two cysts connected with the teeth.

There was no tumour in the cavity.

The X-ray and operation appearances of the cyst in the left body closely resemble that of a "Solitary Bone Cyst in the Mandible" (Rushton, M.A., 1946, *Brit. dent. J.*, 81, 37); but in this case there are also two other similar cystic areas—one in the same region of the right body and one in the region of the symphysis.

Ætiology: The ætiology of "Solitary Bone Cysts" is obscure, but most explanations include trauma as the exciting cause. The only history of trauma in this case is the fall on the chin at 2½ when the front teeth were broken. According to Rushton there are three main hypotheses as to how the trauma may act: (*a*) intramedullary arterial hæmorrhage resulting in a blood cyst; (*b*) injury to the main endosteal artery resulting in loss of vitality in the area most remote from a collateral circulation; (*c*) a subperiosteal hæmatoma with temporary severance of the cortical circulation, osteoclastic absorption towards the cortex from the medulla, this in turn contained later by the restored cortical bone—the end-result being either a cyst or a giant-celled tumour.

The third view (*c*) brings the ætiology into line with the observed pathology of osteitis fibrosa. In 1938 (*Proc. R. Soc. Med.*, **31**, 1141) I demonstrated that microscopic views of different areas in the same case could give the appearance singly of (1) the typical resorption of bone and replacement by fibrous tissue, of osteitis fibrosa, (2) new bone formation taking place in fibrous tissue, suggestive of osteogenic sarcoma, (3) an intervening stage, after resorption, where the whole field is very rich in giant cells, suggestive of a myeloma.

18.9.46: *Later treatment.*—Swelling of gum almost subsided after one week. Hard bony expansion of outer plate below $\overline{|56}$ just palpable but scarcely visible. $\overline{|4567}$ unresponsive to tests for vitality.

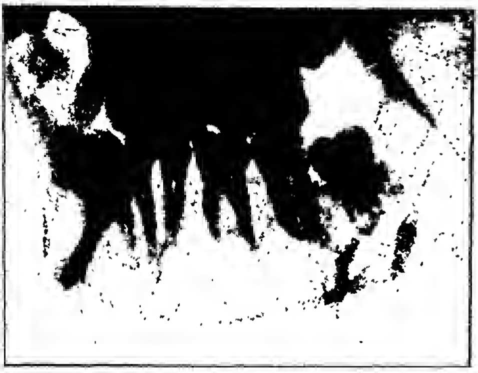


FIG. 1.

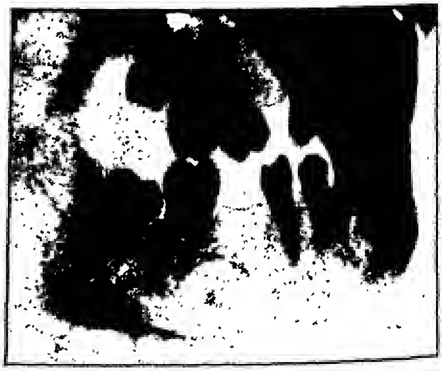


FIG. 2.

Fig. 2.—X-ray of right lateral jaw for control purposes. Irregular cystic area below $\overline{76|}$ region, with an island of sclerotic bone in the centre. The mental foramen lies just forward below root of $\overline{5|}$.

$\overline{6|}$ had been extracted six months earlier; sockets completely filled. $\frac{8|}{8|}$ unerupted, in normal position.

Fig. 3.—X-ray of symphysis, intra-oral: clearly-defined cystic area below $\overline{21|}$ unconnected with the teeth. The lines of the lamina dura and periodontal membrane are unbroken.

$\frac{|6}{|7}$ were extracted under N_2O+O_2; and it was evident that the socket of $\overline{|7}$ did *not* connect with the cyst below; the infection had only involved the soft tissue covering the $\overline{|8}$.

The patient's blood calcium and phosphorus were normal as was also the X-ray of all long bones.

25.9.46: Operation under general intratracheal anæsthetic in a clean field. $\overline{|56}$ extracted—no connexion with cyst (the extraction of these teeth could have been avoided if the cyst had been opened first). Gum flap reflected downwards towards buccal sulcus and bony window in outer plate below sockets of $\overline{|567}$ removed. The cavity in the bone now clearly exposed—no infection, no lining membrane, no contents. Inner surface of the bone was bare and smooth. The nerve was apparently lying uncovered in the floor. The gum flap was turned into the floor and the cavity packed.

There was nothing to send for pathological examination.

28.10.46: Uneventful convalescence. Rapid granulation and epithelialization of cavity. Obturator fitted. Later X-rays show regeneration of bone and filling in of cavity.

24.3.47: Clinically the cyst cavity has completely filled in, six months after operation.

There is a very considerable increase in the consumption of cereals (including bolted wheat flour and biscuits). The consumption of sugar has reached—and at some trading stations even surpassed—the top levels of countries like the United States and Denmark.

Greenland is a closed country. Nobody can go there without the permission of the Danish Government. All trade with the natives is a State monopoly. The turnover of all goods is on record and well known. Useful information is obtainable from the Colonial Administration on the sale of food by each trading post as well as on many other aspects of native life.

Under the joint sponsorship of the Danish Government, the Dental School in Copenhagen, and the P. Carl Petersen Foundation the author, with a varying number of co-workers, made three expeditions to Greenland in order to study dental conditions and allied subjects.

During 1935 motor-boat journeys covering more than 1,500 miles took the author all over the Julianehaab district, South-west Greenland, in which about 25% of the West-Greenlanders are living. A total of 1,634 natives representing all degrees of urbanization were examined. On top of this a good deal of dental treatment was done.

During 1936 the author examined teeth and jaws of 525 Eskimo skulls from Greenland in the Copenhagen University Institute for Medical Anatomy.

During 1937 East Greenland had its first experience of dental surgeons. 915 Eskimos (i.e. 96% of the population) were examined. X-ray series were made of 140 Eskimo jaws, and casts were made of 150 native dentitions.

During 1939 the third Danish dental expedition to Greenland visited the Julianehaab district, South-west Greenland, to re-examine the natives there. Four dental surgeons and a biochemist participated in the work which included clinical, biochemical, X-ray and other studies of about 700 natives. Part of the saliva studies were made in collaboration with Drs. Karshan, Siegel and Tenenbaum of the Columbia University, New York (*J. dent. Res.*, 1940, **19**, 303). Further objects of biochemical studies were viscosity of saliva, inorganic phosphate and calcium of saliva, caries susceptibility (Fosdick tests), inorganic phosphate and ascorbic acid contents of the blood (Farmer and Abt).

The following are some of the principal results of the aforementioned dental investigations.

DENTAL ANATOMY

The Eskimo dentition exhibits a number of characteristic features the more interesting of which are given in the following paragraphs:

The crowns of the molar teeth are superior in size to those of whites whereas the crowns of premolars, canines, and incisors are not. This is noteworthy in so far as it shows that the proportion of size of the crowns is not necessarily the same within the dentitions of all ethnic groups.

The third molar is vestigial in a very high proportion of pure-bred Eskimos and congenitally missing more often in the East Greenland Eskimo than in any other group on record.

Shovel-shaped incisors are almost universally met with.

Cusp numbers and occlusal pattern of the molars come closer to conditions found in fossil apes such as *Dryopithecus* than do cusp numbers and occlusal pattern in other modern racial and ethnic groups hitherto studied. The lower second molars are quintitubercular in a high percentage of cases.

Prognosis: The opening of these cysts allows rapid growth of new bone to take place and the cavity fills in; this has already happened in this case after six months.

The patient will be kept under careful observation; any sign of activity in the two unopened cysts will indicate surgical interference.

[*April 14, 1947*]

Dental Investigations of Greenland Eskimos. [*Summary*]

By P. O. Pedersen
Associate Professor of Dentistry, Copenhagen.

Greenland is the largest island in the world. The greater part of the country is covered with ice. The ice cap completely separates East Greenland from West Greenland. Greenland has only 17,000 inhabitants, of whom approximately 1,000 live on the eastern coast.

During the greater part of the year *East Greenland* is isolated from the outside world by an impenetrable ice girdle. All the natives of East Greenland live in the areas around the trading stations of Angmagssalik and Scoresbysund. The Eskimos at Angmagssalik were unknown till 1884 when the tribe was discovered by an officer of the Royal Danish Navy. In 1894 the Danish Government established a trading station at Angmagssalik to prevent the natives from perishing. The Scoresbysund area became inhabited in 1924 by Eskimos emigrating from Angmagssalik. The Eskimos of East Greenland are practically without white admixture. In remote parts of the Angmagssalik area they still largely subsist on Eskimo protein-fat diet and—at most—taste white man's food. The Eskimos who have settled down at the two trading stations, however, have to no small extent adopted the dietary habits of white men.

Contrary to East Greenland *West Greenland* had early white contact and Danish colonization was firmly established more than two hundred years ago. The western coast is more easily accessible than is the eastern coast and white influence is more predominant. The natives, among whom are a large number of mixed blood, have settled down under urbanized conditions and largely depend on imported food. This is especially true of the main trading stations. The degree of urbanization in the native villages entirely depends on the distance to and accessibility of the trading post. In 1901 the estimated calorie requirement of the West Greenland population was covered to the extent of 17% by imported food. In 1930 the import covered 63% of this requirement. The latter amount being an average for trading stations and villages, the extremely high proportion of imported food in the diet of the West Greenland trading-post natives clearly stands out. In some areas it even surpasses 90%. The radical and sudden change of nutrition which has taken place in West Greenland during the past thirty to forty years is illustrated by the figures in Table I.

TABLE I.—AVERAGE YEARLY CONSUMPTION OF IMPORTED VICTUALS IN WEST GREENLAND
(*Kilos Per Head Per Year*)

	1855-1856*	1901-1903†	1930-1933†
Fats	—	0	5·4
Cereals	15·3	33·3	92·2
Vegetables	—	2·2	1·6
Dried fruits	0·5	1·4	6·3
Sugar (and chocolate) ..	3·7	5·0	39·5

*According to Rink.
†According to Bertelsen.

Dental fluorosis was not observed except for a number of cases near the cryolite mine of Ivigtut, South-west Greenland. The natives concerned had absorbed cryolite (Na_3AlF_6) during their early childhood while living close to the mine. A few cases were also observed of which it could be proved that their mothers ten to twenty years ago used to mix their snuff—to which they were very much addicted—with cryolite powder. In this extraordinary way the mothers seem to have absorbed sufficient cryolite so that breast-fed young natives showed mottling of their teeth (for further details—*see Dtsche zahnärztl. Wschr.*, 1940, 43, 623).

TRAUMATIC LESIONS OF THE TEETH

The Eskimo puts great demand upon his teeth. Mastication is strenuous and the teeth are used as a tool for many kinds of work. The women use their teeth for preparation of seal hides. The hides are thoroughly chewed. This applies for instance to the hides to be used for boot-soles. Sinews are pulled across the teeth and rolled against the cheek to make them apt for sewing. Prepared in this way the sinew will wear a groove in the " masticatory surfaces" of the incisor teeth. This groove has a transverse course and remains somewhat ahead of the general attrition.

The general attrition of the teeth is severe during maturity and in the old Eskimo—male as well as female—the teeth are often worn down to the gums. In females the chewing of hides accounts for part of the wear. On the whole, however, the bearing of this kind of work upon the attrition of Eskimo teeth has been overemphasized since the male Eskimo, who does not chew hides, also shows exceedingly pronounced wear of his teeth.

Exposure of the pulp due to attrition is comparatively rare. In most cases abundant formation of secondary dentine protects the pulp cavity from being opened.

Multiple small fractures of the teeth are seen in almost all adult Eskimos living in primitive areas. Extensive fractures exposing the pulp are rather frequent.

DENTAL CARIES

We do not know of any case of caries in Eskimo skulls dating with certainty before contact with white people. Among 525 Greenland Eskimo skulls with 5,606 permanent and 146 deciduous teeth only two were found with caries. These two cases are, however, not properly dated and may be more recent than early white contact. They have two and one of the third molars affected respectively. Caries incidence in the total skull collection examined thus amounts to a few permanent teeth per thousand, and no deciduous teeth are affected. This is about the same magnitude of caries incidence as that reported by Mummery who examined 69 Eskimo skulls (*Trans. odont. Soc. Lond.*, 1870, 2).

The principal facts which can be derived from our studies of present-day Greenlanders are the following:—

Caries incidence has risen from nil or practically nil in the pre-Danish time to a considerable level in modern East Greenland and to a simply alarming level in modern West Greenland (fig. 1). This increase has mainly taken place during the last fifty years in West Greenland. In East Greenland it is quite recent.[1]

Caries in villages as well as in trading stations is much more frequent and of a much more severe type in (civilized) West Greenland than in (primitive) East Greenland (fig. 1).

Both in West Greenland and in East Greenland one finds a great difference in the caries incidence in villages on the one hand and in trading stations on the other. The trading stations are everywhere more seriously affected (fig. 1).

---

[1] Incidence of dental caries according to sex, age and locality, *Dent. Rec.*, 1938, 58, 191.

The tubercle of Carabelli—present in about 75% of whites if we include the groove—is almost entirely absent in the Eskimo of unmixed descent. In West Greenland hybrids about one-third of upper first molars exhibit Carabelli's cusp or groove.

Paramolar and distomolar tubercles of Bolk, i.e. supernumerary buccal and lingual cusps on molars, are frequent.

There is a tendency for the Eskimo to develop small pearl-like excrescences on the occlusal surfaces of premolars and molars as well as on the lingual aspects of the canine cusps.

Buccal pits and grooves on lower molars are frequent and quite often pronounced. They may be surrounded by a hypoplastic area, especially so in the primitive Eskimo.

Enamel extensions from the gingival margin opposite root bifurcations and grooves (originally described by Leigh in Eskimos, Indians, and Polynesians and dealt with in England by Watson and Woods) are normal in the Eskimo of Greenland. Such extensions are frequently present to an extreme degree. They are closely related to enamel nodules which are found on upper third and second molars in a much higher percentage of cases than in whites. As many as 25% of upper third molars exhibit enamel drops distally and/or mesially. This seems to be far the highest incidence recorded for any group.

Average root height is reduced during lifetime to a striking degree. In many cases root absorption of vital incisors occurs even during adolescence. More or less pronounced absorption of the apical part of the roots with hyperostosis of the remaining part of the roots seems to be an almost normal occurrence in the primitive Eskimo. Cases have been observed indicating that function can become so strenuous that the parodontal tissues respond with root absorption on a large scale.

Supernumerary roots are frequent. On the lower first molars disto-lingual roots are found ten times as often as in whites (Bolk). High incidence of this root has been reported by Professor Tratman of Singapore in Mongols living in Malaya.

Failure of root-branches to divide is common. Such fusion is similar to that found in certain specimens of early man in Europe. The Eskimo also exhibits a moderate degree of taurodontism, the condition dealt with by Sir Arthur Keith and Professor Middleton Shaw. The pulp cavity is large during childhood and young adult age. Later on secondary calcifications including enormous pulp stones are widespread. Large pulp stones suggestive of vitamin-C deficiency are also found in young teeth.

Our studies of Eskimo tooth morphology confirm that the Eskimo is closely related to the Mongolian stock with which he shares at least the following features: (1) High incidence of shovel-shaped incisors; (2) Very low incidence of Carabelli's tubercle; (3) High incidence of three-rooted lower molars.

Incidence and type of dental numerical variations—omitted in this paper—point in the same direction (*Acta odont. Scand.*, 1939, **1**, 93–134).

DENTAL STRUCTURE

In the primitive Eskimo very few cases of gross enamel hypoplasia are met with. Not a single case of pits and grooves in the incisors has been seen in such groups. Rickets is unknown in the primitive Eskimo. The degree of mineralization as indicated by the surface texture is generally perfect both in the skulls and in present-day East Greenlanders. Among the young West Greenlanders slight M-hypoplasia (classified according to standards kindly supplied by Lady Mellanby) has been observed to a certain extent.

It is a new disease in Greenland leaving the older natives less affected than the younger. However, caries may attack even natives whose teeth have developed under Stone Age conditions. Adult natives leaving primitive localities and settling down in urbanized areas—especially when young—frequently become afflicted with rampant acute caries although their teeth are of perfect structure. This applies, for instance, to young Greenlanders who temporarily stay in Denmark.

A close study of conditions in East Greenland seems to indicate that caries in this area will not occur to a greater extent when imported food amounts to about 20% of the native diet than when this figure is 5%. If, however, the total intake of imported food averages 80%, caries incidence in the permanent teeth will be of the magnitude shown in fig. 1 for the trading station of Angmagssalik.

In the author's opinion we are not entitled to draw far-reaching conclusions from these studies as to the point so much debated in this country, viz. whether the tooth structure or the carbohydrate factor plays the greater rôle. Those who hold the latter view may find some support in our findings, but there are also hints to the opposite effect. Generally speaking, the author does not think that field studies of the kind here presented will definitely solve the caries problem. In all probability the final solution will have to depend on pure experiment. However, we need a sound basis for discussion. As far as caries is concerned our principal aim has been to provide facts for such discussion from a remote corner of the world governed by Denmark.

PARODONTAL DISEASE

In the primitive Eskimo of East Greenland we have not observed any cases of generalized parodontal disease. Nor did we find any in West Greenland. Apparently this dental ailment will enter urbanized groups later than caries. This statement, however, is only true of marginal parodontal disease affecting the bone to such an extent readily detected by means of X-rays. Gingivitis was widespread also in East Greenland. Here the gum disease, however, did not affect the marginal parodontal bone to any appreciable extent. On an average the men were afflicted with gingivitis in greater numbers and also to a more severe degree than were the women. This is, among other things, to be put down to the fact that the men are still more addicted to the use and abuse of tobacco and tobacco ash than the women. Another gingivitis-producing factor, no doubt, is the very frequent mouth-breathing. Ulcerative gingivitis was absent in Greenland during the late thirties.

Loose teeth are only met with in the primitive Eskimo under very special conditions. In one case the lower incisors were loose because their antagonists had been lost at an early date due to an accident, which means that from want of use the teeth may become loose. Excessive use results in loosening of the teeth only when the roots have become so shortened by attrition from the one end and by root absorption from the other that only short stumps not surrounded by bone are left.[1]

Localized traumatic injuries of the marginal parodontal tissues as well as food impaction in connexion with severe attrition are conditions responsible for the loss of some molars in the primitive Eskimo. In modern East Greenland and in some West Greenland villages the use of tobacco-ash-quid ("eroq") produces a localized severe chronic marginal parodontal disturbance around the lower molars of many middle-aged and old people, females as well as males. The ultimate result is loss of one or more teeth (*Paradentium*, 1941, **13**, 25).

---

[1] For further details on parodontal disease see *Paradentium*, 1940, **12**, 69.

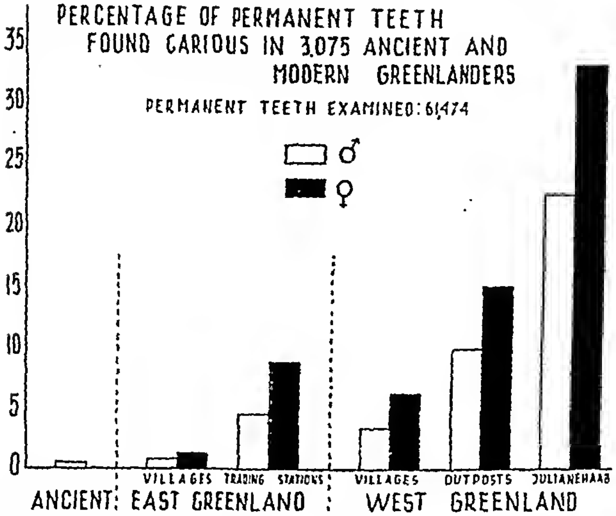


FIG. 1.—Summary of caries incidence in the permanent dentition of ancient and modern Greenlanders 1935-1937. Outposts are small trading stations. Julianehaab is a main trading station.

The natives employed and salaried by the Colonial Administration are everywhere more seriously affected than are hunters of the same age and locality (fig. 2).

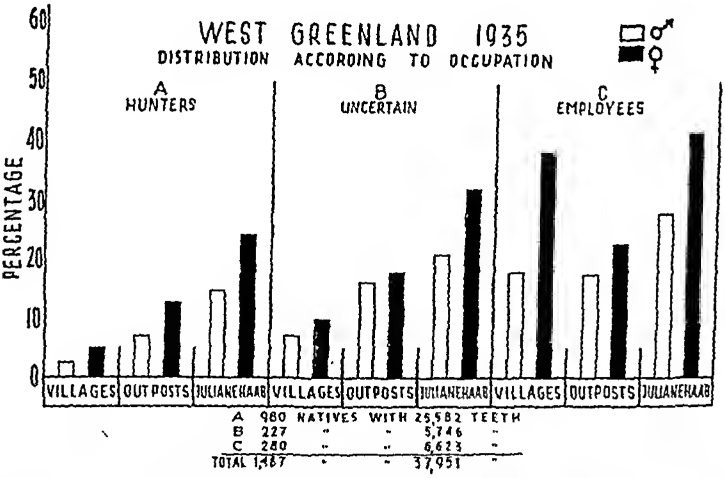


FIG. 2.—Incidence of dental caries in 1,487 West Greenlanders according to occupation. Percentages of carious permanent teeth. Outposts are small trading stations. Julianehaab is a main trading station.

Young natives, *ceteris paribus*, are more seriously affected than are middle-aged and old natives. Caries is a new disease in Greenland.

From whatever angle these principal results of the gigantic nutritional experiment forced upon the native population of Greenland are surveyed it is beyond doubt that the natives who abandon the dietary habits of their ancestors and adopt white man's industrialized carbohydrate food are those who become afflicted with caries.

Caries, which for clinical, biochemical and bacteriological reasons seems to be basically the same disease in the Eskimo as in whites, is seen to be largely independent of racial mixture, since the same rise occurs in the East and West Greenland groups.

Section of Medicine

President—Maurice Davidson, M.D.

[*March* 25, 1947]

Painful Disability of the Shoulder in Coronary Disease

By A. Schott, M.D.

From time to time patients with coronary disease are seen in whom the outstanding symptom is a painful disability of one or both shoulders resembling scapulo-humeral periarthritis. If this occurs a short time after an attack of coronary occlusion during which pain radiated to the affected shoulder the condition may wrongly be considered to be just the usual manifestation of myocardial infarction, and not being recognized as a separate lesion, appropriate treatment is not considered, or is delayed. If, on the other hand, periarthritis is diagnosed, the question arises: what relationship, if any, exists between coronary disease and periarthritis of the shoulder?

So far, this question seems to have attracted attention chiefly amongst cardiologists and is not considered in papers on periarthritis (Dickson and Crosby, 1932; Douthwaite, 1938) or discussed in textbooks on orthopædic surgery (Jones and Lovell, 1929; Whitman, 1930; Tavernier, 1937; Mercer, 1943). In his monograph on the shoulder Codman (1934) actually disagrees with the view that referred pain in coronary (and other) disease can produce limitation of movement or true localized tenderness in the scapulo-humeral joint. Only Moseley (1945) seems to have listed chronic cardiac disease amongst the general conditions which may produce scapulo-humeral periarthritis.

However, perusal of papers dealing with this subject from the cardiological angle (Howard, 1930; Edeiken and Wolferth, 1936; Boas and Levy, 1937; Leech, 1938; Ernstene and Kinell, 1940; Spillane and White, 1940; Askey, 1941) leaves little doubt that, at least in quite a number of cases, a definite relationship seems to exist between coronary disease and periarthritis of the shoulder and this association does not appear to be very rare; Ernstene and Kinell found it in 12% of 138 cases of myocardial infarction, and Fishberg (1940) was so impressed with the frequency with which cardiac pain manifests itself exclusively in the shoulder that in his opinion the practitioner should bear the possibility of coronary disease in mind "in all middle-aged individuals who complain of pain and limitation of movement in the shoulder, *especially the left*". As, however, both conditions are common in patients over 40 investigations of the cardiac condition of a larger number of patients with this kind of shoulder lesion are required, to throw light on the frequency and nature of the association between the two conditions.

A short report is presented on 6 patients who were seen in cardiological practice and who had coronary disease associated at one time or another with a painful disability of the shoulder.

Case I.—Male aged 52. Eight years' history of intermittent claudication, five years of angina of effort with pain in the left chest and left arm, one month of nocturnal angina of rest, relieved by trinitrin, but some pain in the left axilla persisting continually.

On examination (25.1.43).—Moderate emphysema of the lungs and hyperpiesia; B.P. 175/100. *Resting E.C.G.:* R absent in CR_3; otherwise normal. Anginal pain and marked electrocardiographic signs of myocardial anoxia in the limb leads after a small amount of exercise. One week

IRREGULARITIES OF TOOTH POSITION

Perfect development of the jaws and regular position of the teeth were predominant in ancient Eskimos and are still so in present-day East Greenlanders. Irregularities are, however, not at all rare with the latter. This not only holds good of young natives, but also of adults who have, during their childhood, practically never seen a white man, still less lived on white man's food. These irregularities (mainly crowding of upper and lower anteriors as well as irregularities in the premolar regions) have nothing to do with the crowding of the upper incisors observed by Weston A. Price in semi-civilized and civilized peoples in various parts of the world and so energetically maintained by him to be caused by civilization.

Failure of eruption of permanent teeth is not infrequent, and the author has observed several cases of aberrant eruption or impaction (*Tandlægebladet*, 1943, 47, 1). Impactions of lower third molars are fairly common, but do not seem to be associated with lack of space for the accommodation of the wisdom teeth.

In 1931 Sir Arthur Keith in his foreword to Professor Middleton Shaw's book on the dentition of the South African Bantu, said:

> "The greater part of the world still remains in a state of dental darkness. Even in Europe and America much still remains to be done to complete a preliminary survey of the mouths of mankind. . . Teeth are key structures—providing clues to race and to bodily health. Our knowledge of man's past has to be based very largely on a study of fossil teeth and jaws. . . .Teeth are more susceptible than other structures of the body to the changes which are produced by civilization. . . .We cannot know too much about teeth."

In 1947 we have not gone much farther than when these words were written. We have still many lessons to learn from the study of dental conditions in primitive peoples all over the world.

to exertion or emotion and does not respond to trinitrin. In the acute form the shoulder is diffusely tender and may be extremely painful, particularly at night, the pain being continuous and described as dull, burning or wrenching. The arm feels heavy, leaden, useless. The shoulder may be quite immobile, "frozen", owing to muscle spasm, the patient resenting even the slightest movement and carrying the arm in a sling. In the less acute stage there is pain only on certain movements, chiefly abduction and external and internal rotation, and there is limitation of these movements. If these persist after the acute stage has completely subsided, they are due to adhesions, particularly in the subdeltoid bursa. Putting on a coat or brushing the hair involves movements most readily affected. It is not proposed to discuss in further detail the symptomatology of periarthritis (*see* Douthwaite, 1938) or the various conditions which sometimes are summarized under the name of periarthritis (*see* Burns and Ellis, 1937; Moseley, 1945).

In all patients of this series anginal pain with or without signs of myocardial infarction preceded periarthritis, the interval varying between a few weeks and five years, though in Case IV there was a dull continuous ache in the left upper arm for one year prior to an attack of coronary occlusion. Shoulder pain, however, may precede coronary occlusion (Spillane and White, 1940; Askey, 1941), though this is less common.

It has been observed by various authors that in cases with left-sided anginal pain the left shoulder tends to be affected, whereas with right-sided radiation of the anginal pain the right shoulder is more commonly involved. The present small series illustrates this relationship well: of the 4 cases where the left shoulder was affected (in 3 exclusively and in 1 predominantly) anginal pain was left-sided in 3, and in the mid-line without radiation in the remaining 1; of the 2 patients with periarthritis on the right the anginal pain had involved the right chest in 1 and in the remaining 1 had radiated into both arms, chiefly into the right one. Although perusal of the literature shows that this relationship does not exist in all cases, the predominance of the left shoulder in cases of periarthritis with coronary disease is striking; amongst 114 published cases of this kind the left shoulder was affected in 65, the right in 34 and both shoulders in 15. On the other hand, in a series of 200 cases of periarthritis of the shoulder without any reference to coronary disease the right shoulder was affected in 103 cases, the left in 84 and both in 13 (Dickson and Crosby, 1932), and in Douthwaite's series of 37 patients the right shoulder was affected in 21, the left in 15 and both in the remaining 1. There is also a striking difference in the sex incidence between patients with and without coronary disease. Periarthritis as seen by the orthopædic surgeon seems to occur with equal frequency in the two sexes (Dickson and Crosby, 1932) and in Douthwaite's series 22 of the 37 patients were females; this contrasts with a marked preponderance of males in patients with coronary disease and periarthritis : of 68 published cases in which the sex of the patient was stated 50 were males, i.e. a preponderance of males of nearly 2·8 : 1. Moreover, the appearance of periarthritis in such cases has been observed often to coincide with, or shortly follow, an increase in anginal pain.

There seems little doubt that some relationship between these two conditions exists although the mechanism is obscure. Some suggestions about its possible nature are contained in Ernstene and Kinell's paper (1940).

The recognition of a possible relationship in patients over 40 between scapulo-humeral periarthritis, particularly on the left, and coronary disease is important. In patients known to be suffering from coronary disease or who have had an attack of coronary occlusion the appearance of a painful disability of the shoulder in which pain had previously been experienced may lead to the erroneous assumption that the patient had a recent attack or recurrence of coronary occlusion. A further period of rest in bed which would then be advised is unnecessary and, if anything, tends to prolong the disability of the shoulder. If periarthritis precedes anginal pain it may be a sequel to an unrecognized attack of coronary occlusion, or it may be the first symptom of coronary disease. A complete cardiological examination may then reveal the presence of hitherto unsuspected coronary disease.

The treatment of this condition may be very difficult. It seems to clear up by itself after some months but sometimes it persists for years. No single method of treatment has yet proved generally successful and there is hardly a kind of physiotherapy which has not been suggested. In the acute stage the exhibition of morphia may be necessary, especially to ensure sleep, as the pain tends to be particularly severe at night. The arm should be rested in abduction. Infiltration of the painful area with 1% procaine without adrenaline, not exceeding 8 c.c. at one sitting, repeated daily, and combined with calcium aspirin, 15 grains q.i.d., seems to deserve a wider application. When the acute stage has subsided physiotherapy in a form suitable to the individual is indicated. Carefully graded active and passive exercises are important in order to prevent adhesions. Deep X-ray treatment which produced good results in Case I has been reported without success in other cases; diathermy gave good results in some. Manipulation under an anæsthetic, which is contra-later continuous pain started in the left shoulder, radiating down the whole of the left arm and into the left hand, associated with stiffness of the second and third fingers. An X-ray of the shoulder did not show any abnormalities. The patient was admitted elsewhere to a hospital where eight short-wave treatments and wax baths were given without success. *On re-examination*, three and a half months later, the patient complained of continuous severe pain in the left shoulder, worst at night and impairing sleep in spite of morphia. The shoulder was "frozen", hardly any movement being possible without producing excruciating pain, and there was also some limitation of extension in the left elbow. There was marked tenderness over the anterior aspect of the shoulder-joint and the insertion of the deltoid as well as, to a lesser extent, over the elbow and thenar. Subdeltoid bursitis was diagnosed by an orthopædic surgeon who advised careful manipulation under an anæsthetic; this greatly aggravated the condition and when seen again five months later the patient complained of even more severe pain in the shoulder, particularly at night, carried the arm in a sling, and resented the slightest attempt at any movement. He then also complained of pain in the knees and hips, particularly on the left, and there was limitation of movement in the left hip-joint. At the same time, he had more severe substernal pain at rest, relieved by trinitrin which had no effect on the shoulder pain.

The patient was referred to Dr. Douthwaite who diagnosed scapulo-humeral periarthritis of both shoulders, more advanced on the left, with adhesions particularly in the subdeltoid bursa, and fibrositic changes in the region of the left hip-joint. The sedimentation rate was normal. He advised infiltration of the tender muscles with 1% procaine without adrenaline, starting with the left deltoid, calcium aspirin and subsequently treatment by deep X-rays. This treatment resulted in such marked improvement that on re-examination five months later pain and disability in the shoulder had completely disappeared, but pain in the hips on walking had become more marked.

CASE II.—Male aged 64. Eighteen months' history of angina of effort (substernal pressure without radiation, and choking), with three attacks of cardiac asthma. Raised blood-pressure for ten years.

On examination (19.3.43).—Congestive heart failure, auricular flutter with varying block; X-ray: considerable dilatation of the heart with grossly enlarged left ventricle and congestion of the lungs. With appropriate treatment the condition improved until January 1944, when cardiac asthma and angina of rest recurred. By readjusting the dose of digitalis the cardiac condition improved, but three days later pain in the left shoulder started and on examination there was limitation of abduction, external and internal rotation. An orthopædic surgeon (Mr. L. S. Michaelis) reported: Slight wasting of the left deltoid, supra- and infraspinatus muscles, slight tenderness on pressure over the anterior aspect of the joint, limitation of abduction to 60 degrees, of external rotation to 10 degrees and internal rotation to 25 degrees. No signs of acute inflammation. The suggested treatment was radiant heat, gentle massage and passive and active exercises, but all treatment had to be discontinued. The pain disappeared gradually without any treatment in the course of a few weeks. He died suddenly in February 1946.

CASE III.—Male aged 43. Attack of coronary thrombosis in August 1944 with pain across the left chest radiating into both arms, chiefly into the right. Pain in the right shoulder on moving the right arm started eight weeks after the attack. In Spring 1945 this pain occurred also without moving the arm and, in addition, affected the right forearm and a small area in the third and fourth interspaces in the anterior axillary line of the right chest. He was referred for a cardiological examination as the appearance of shoulder pain led to the assumption that another attack of coronary thrombosis might have occurred. On examination, there was no clinical or electrocardiographic evidence of coronary occlusion, but tenderness over the right trapezius, below the coracoid process, over the right upper quadrant of the right chest and the right upper arm. Backward movement of the right arm produced pain of the same character and distribution as the pain which occurred spontaneously. Fine crepitations were palpable over the right shoulder. One treatment by gentle manipulation without an anæsthetic by a physiotherapist followed by massage and active exercises produced rapid improvement. *On re-examination* (17.12.45) the pain had disappeared and all movements were normal.

CASE IV.—Male aged 67. Contracted syphilis at the age of 22, serological tests consistently negative. Angina of effort for two years, and pain in the left upper arm not related to exercise for one year, prior to an attack of coronary thrombosis in July 1944.

On examination (24.11.44).—E.C.G. Q_1-T_1 type of old infarction. No complaints except for some slight pain in the left shoulder on backward movement (putting on coat) which had started a few weeks after the attack of coronary thrombosis and had persisted ever since. There was slight limitation of abduction and internal rotation which had remained stationary during several subsequent re-examinations. 7.2.45: Recurrence of slight præcordial discomfort on exertion, relieved by trinitrin which had no effect on the shoulder pain.

CASE V.—Male aged 56. Periarthritis of the left shoulder three weeks after an attack of coronary thrombosis with pain in the left chest and left shoulder.

CASE VI.—Male aged 49. Periarthritis of the right shoulder three years after an attack of coronary thrombosis with pain in the right chest.

Detailed description of Cases V and VI is omitted owing to lack of space.

Discussion.—The clinical features of the painful disability of the shoulder closely resemble those of scapulo-humeral periarthritis, the post-traumatic form of which was first described by Duplay in 1872; trauma, however, played no part in these cases. The condition is distinct from the common radiation of anginal pain to the shoulder region: it is not related

Markedly enlarged mediastinal glands are rare in whooping cough and play little part in the production of pulmonary collapse.

The part played by tuberculous mediastinal glands is difficult to assess. Occasionally bronchoscopic examination reveals obvious bronchial occlusion due to pressure from without, fibrous stenosis or caseous material, but more often cases present with permanently damaged collapsed lower lobes and radiological evidence of hilar calcification. In this latter group, bronchoscopy usually shows no abnormality and one is tempted to assume that tuberculous glands were at least partly responsible for the original bronchial occlusion.

Infections of the nose or throat, principally chronic antral infections, were found in 16 of the present series of 50 cases. They occurred mainly in association with collapse of long-standing and saccular bronchiectasis. Their chief importance was to act as a source of septic material which, on aspiration, gave rise first to pulmonary infection and later to permanent changes in the lower lobes after they had collapsed.

Lobar collapse may arise in two ways, either by failure of expansion of the lobe at birth or by bronchial occlusion with subsequent absorption of air distal to the obstruction. It may be impossible to distinguish between these two mechanisms in any given case, but the frequency with which collapse is seen to occur in pulmonary affections and its rarity as an incidental finding in children dead of non-pulmonary diseases, confirms the view that the condition is acquired after birth in the great majority. Occasionally, the cause of the obstruction is obvious, as by foreign body, ulcerating tuberculous mediastinal gland or viscid post-operative secretion. Far more often, however, the collapse appears to date from an attack of pneumonia, bronchitis, whooping cough or measles, in which case the most important precipitating cause is bronchial secretion.

On the right side, should the obstruction occur in the main descending bronchus, the whole of the middle and lower lobes collapse; if the secretion subsequently be drawn beyond the orifices of the bronchi to the middle lobe and the dorsal segment of the lower lobe, one or other or both of these may re-expand, leaving the basic segments collapsed. On the left side, collapse of the lingular process is less commonly associated with collapse of the lower lobe than is collapse of the middle lobe on the right side, the probable explanation being that the point of origin of the bronchus to the lingular process is normally from the bronchus to the antero-lateral segment of the upper lobe. It is common experience that the left lower lobe collapses more frequently in children than does the right. Figures for this series were: Left 28; right 18; bilateral 4. This difference may be related to the close proximity of the arch of the aorta to the larger bronchi on the left side leading to kinking of the bronchi by degrees of mediastinal glandular enlargement which would not produce such kinking on the right.

Re-expansion occurred in only 10 of the 50 cases during the period of observation; this figure is misleading as many cases of persistent collapse are referred to chest hospitals for treatment of established bronchiectasis, the collapse being an incidental finding, consequently no true incidence of re-expansion can be deduced. When it occurs, re-expansion is nearly always complete within two months of the diagnosis having been made—it is very rarely seen after more than six months in the absence of an obvious obstruction to a large bronchus. There is no reason why collapse should not persist for years and then be followed by complete re-expansion in the absence of infection; this is seen not infrequently in suitably treated cases of spontaneous pneumothorax or giant cyst of the lung. In the case of the lower lobes, however, collapse persisting for more than a few months is almost invariably complicated by permanent inflammatory changes due to the accumulation of septic material in the bronchi. In the 40 cases which failed to re-expand, bronchiectasis was found in the following proportions: Bronchiectasis—saccular 21; cylindrical 16; cystic 1; no bronchiectasis 2.

The time required for the development of bronchiectasis and pulmonary fibrosis is very variable. One case showed gross fibrosis and saccular bronchiectasis at operation eight months after the inhalation of a peanut; another showed mild cylindrical bronchiectasis and little in the way of sputum in association with a lobe which was known to have been collapsed for eight years.

With viscid sputum as the commonest cause of collapse, treatment must be directed towards its expectoration. Postural drainage and expectorants, such as a saline-hot water mixture or inhalations of friar's balsam may be effective in older children but are often difficult of application in babies for whom an oxygen tent is essential. Sulpha drugs or penicillin should be given as a routine and breathing exercises are valuable as an aid to re-expansion after the sputum has been loosened. Bronchoscopy has a place, particularly in older children, and should be performed within a day or so of the development of collapse and after postural drainage has been tried and failed.

In long-standing cases, the treatment is that of bronchiectasis.

indicated in the acute and subacute stages, is the method of choice and often curative when limitation of movement persists owing to adhesions.

Further experience is needed to show how far this method is applicable in coronary disease.

Summary.—Six cases of coronary disease with painful disability of one or both shoulders are described. The condition of the shoulder resembled scapulo-humeral periarthritis. The literature is briefly reviewed and reasons are given for the belief that some relationship exists between the two conditions. It is suggested that examination for coronary disease of larger numbers of patients over 40 with painful disabilities of the shoulder—especially the left—without obvious cause is desirable in order to establish the frequency and nature of this relationship.

REFERENCES

Askey, J. M. (1941) *Amer. Heart J.*, 22, 1.
Boas, E. P., and Levy, H. (1937) *Amer. Heart J.*, 14, 540.
Burns, B. H., and Ellis, V. H. (1937) Recent Advances in Orthopædic Surgery. London.
Codman, E. A. (1934) The Shoulder. Boston, p. 484.
Dickson, J. A., and Crosby, E. H. (1932) *J. Amer. med. Ass.*, 99, 2252.
Douthwaite, A. H. (1938) *Brit. med. J.* (i), 441.
Duplay, S. (1872) *Arch. gén. Méd.*, 20, 513.
Edeiken, J., and Wolferth, C. C. (1936) *Amer. J. med. Sci.*, 191, 201.
Ernstene, A. C., and Kinell, J. (1940) *Arch. intern. Med.*, 66, 800.
Fishberg, A. M. (1940) Heart Failure. 2nd ed., Philadelphia, p. 410.
Howard, T. (1930) *Med. J. Rec.*, 131, 364.
Jones, R., and Lovell, R. W. (1929) Orthopædic Surgery. 2nd ed., London.
Leech, C. B. (1938) *R. I. med. J.*, 21, 104.
Mercer, W. (1943) Orthopædic Surgery. 3rd ed., London, p. 674.
Moseley, H. F. (1945) Shoulder Lesions. Springfield Ill., p. 66.
Spillane, J. D., and White, P. D. (1940) *Brit. Heart J.*, 2, 123.
Tavernier, L. (1937) in Ombrédanne and Mathieu, Traité de Chirurgie Orthopédique, Paris, 3, 2168.
Whitman, R. (1930) Orthopædic Surgery. 9th ed., London.

Collapse of the Lower Lobes of the Lungs in Children

By Neville C. Oswald, M.D., F.R.C.P.

Fifty cases of collapse of the lower lobes of the lungs in children were collected from the records of the Brompton Hospital, the sole criteria for selection being that they were adequately investigated and that there was a radiological follow-up of at least six months. Cases showing partial collapse only were excluded.

The average age of onset of pulmonary symptoms was 3 years; in 29, or more than half the cases, pulmonary symptoms started during the first two years of life. The mode of onset of symptoms was as follows:

Pneumonia	17	Tuberculous mediastinal glands	3
Bronchitis	13	Infected antra	1
Whooping cough ..	7	Diphtheria	1
Measles	4	Foreign body	1
Tonsillectomy	3		
	Total 50		

These findings suggest that pneumonia, bronchitis and the specific fevers form the starting point of pulmonary infection which leads eventually to collapse in the great majority. Unfortunately, in nearly all instances, collapse had occurred by the time the first radiograph was taken and, with a long previous history of respiratory disease, it was often difficult to decide how long it had been present. However, as more than half the children had had recurrent pneumonia or bronchitis dating from an acute pulmonary infection during the first two years of life, and in the majority of these permanent structural changes were demonstrated either by bronchography or at operation in the collapsed lobe, it must be presumed that collapse occurred before the age of 2 in a high proportion. Probably the most important single factor in the production of collapse at this early age is the small calibre of the bronchi, enabling plugs of tenacious bronchial secretion to cause bronchial occlusion.

In the past, measles and whooping cough have given rise to much chronic pulmonary infection and collapse. The routine use of sulpha drugs has greatly reduced the incidence in measles but in whooping cough serious pulmonary complications are to be expected in not less than 10% of cases, largely as a result of collapse produced by tenacious mucoid sputum.

(3) Apparently specific to osteomalacia are small irregular spaces in the cancellous bone of the vertebræ; which also show well the bulging of the intervertebral discs into the osteoporotic bodies.

The differences found on pathological examination in fœtal rickets, infantile rickets, adult rickets and osteomalacia are those due to differences in the skeleton, rate of growth, and amount of decalcification, with the formation of fibre bone (i.e. derived from fibrous tissue) in the child, and to a much less extent in the adult.

Chemical pathology.—In a well-marked case of osteomalacia there are certain chemical changes: (*a*) The serum calcium is low, 5 to 8 mg%. (*b*) The inorganic phosphorus is low, 1 to 2·5 mg%. (c) The phosphatase units per 100 c.c. are low, 4 to 5. (*d*) The calcium supply in the milk in a parturient woman with osteomalacia is below standard figures.

These figures are paralleled in the child with fœtal rickets and, in the latter case, the hæmoglobin and red cell counts of the cord blood are also below normal.

The urine and fæces show a negative calcium balance, and a positive phosphorus balance.

In the adult the cortex of the bone is poor in calcium; whilst in the analysis of bones from fœtuses born from mothers suffering from osteomalacia, there is a definite calcium and phosphorus deficiency, whilst the relation of calcium to phosphorus remains about normal.

Valuable work has been done by Liu (1935) and his associates in the study of the calcium and phosphorus metabolism in osteomalacia. Some of their conclusions are given below:

"While their basic abnormality of poor calcium conservation because of vitamin-D deficiency remains identical, two types of osteomalacia are recognizable by the levels of serum calcium and inorganic phosphorus, in one type serum calcium is low, but inorganic phosphorus normal, and in the other type inorganic phosphorus is decreased, but calcium normal. In low calcium osteomalacia tetany is the predominant feature and lenticular opacities are often present; while in low phosphorus osteomalacia, the presenting symptoms are bone tenderness and skeletal deformities. Osseous decalcification in the first type may be mild or early, whereas in the second type it is more likely to be advanced.

"In low phosphorus osteomalacia the normal serum calcium may be lowered and the low inorganic phosphorus raised by diets low in calcium and high in phosphorus.

"Both types of osteomalacia respond readily to vitamin-D therapy. When skeletal decalcification is extensive, the improvement in calcium and phosphorus retention is prompt and marked. When skeletal decalcification is slight, such improvement may not be striking. Likewise calcium and phosphorus retention slackens as the bony stores are replenished under treatment.

"After the administration of vitamin D, serum calcium, when low, is raised to normal and its rise is more rapid in the case of slight skeletal osteoporosis than in the case of pronounced decalcification. Serum inorganic phosphorus, when low, rises rather slowly, being susceptible to the influence of factors other than vitamin D."

Another matter also comes under consideration when one deals with the question of associated tetany; i.e. the matter of calcium-ion concentration, for this trouble seems to depend on this rather than on the total serum calcium. If the former is over 4% there is osteomalacia without tetany. Howland and Kramer laid down that if the product of the concentration of calcium and phosphorus in milligrams per 100 c.c. of serum falls below 30, rickets is invariably present in children. The same figure apparently holds good for osteomalacia though it must be remembered that the normal figure in adults for phosphorus tends to be lower than in children.

In the question of the possible prediction of fœtal rickets in a case of osteomalacia; if the product of calcium and phosphorus in the mother's blood, near term, is below 20, the baby will exhibit the signs of fœtal rickets.

Radiological appearances.—In the beginning of the disease little is to be observed. As the disease advances there is decalcification, and the structure of the spongiosa becomes more grossly reticular. The decalcification may proceed to such an extent that satisfactory X-ray films cannot be obtained.

The characteristic changes in the pelvis are easily seen, and in the early cases the yielding of the lateral wall due to pressure about the acetabulum is manifest. Gradually the typical triradiate pelvis is developed, sometimes fairly regular, sometimes with considerable asymmetry, depending to a certain extent on the patient's posture. The edge of the iliac bones tends to flatten and the increased convexity of the sacrum may result in the formation of a sharp angle.

Osteomalacia [*Summary*]

By J. Preston Maxwell, M.D., F.R.C.S., F.R.C.O.G.

History.—Osteomalacia was first recognized as an entity in the middle of the seventeenth century. Lambert wrote on it in A.D. 1700 (Ribémont-Dessagnes and Lepage, 1894).

In 1885 Pommer insisted on the identity of osteomalacia with rickets, countering the view of Virchow that the two were separate entities. Clinical evidence gradually accumulated to show that early rickets, late rickets, and osteomalacia, occurred endemically and at the same time. In 1922 Mellanby (1921, 1925), McCollum (1922) and Hess (1929) proved that for both diseases a deficient vitamin intake was of paramount importance, and shortly after this researches in Peking and India established that this disease is rickets in the adult, and is part of the series, fœtal rickets, infantile rickets, late rickets, and adult rickets. These researches have been confirmed and extended by Snapper (1943) in Peking.

Distribution.—The two world centres in which the disease is now found are parts of India and North China. But given the requisite conditions, i.e. avitaminosis D, one may get it anywhere. It used to be endemic in the Rhine and Danube valleys, especially in the upper reaches.

Both men and women are affected, though on account of the calcium strain of pregnancy, more cases have been seen in women, and parturition may become a death-trap for both mother and child. Race is no barrier to the affection.

General clinical manifestations.—The most common early symptoms both in men and women are pain in the back and thighs, with spasm of the adductor muscles, often accompanied by disturbances of sensation in the hands and feet. The lumbar pain is the earlier, and is of an aching character, worse in winter months and in sunless periods.

At first there is no bone tenderness, but as the trouble progresses, the bones become tender, especially the lower ribs and pelvic girdle, and softer spots may be felt on the ribs. Two forms of pelvic deformity manifest themselves. The first is the formation of a funnel pelvis, and this is apt to take place in cases of late rickets; the second is the typical triradiate pelvis of severe osteomalacia. The sacrum develops an acute convexity, the lower portion and the coccyx coming forward; the chest develops either a lateral curvature with rotation, or a pure kyphosis; the neck sinks into the upper portion of the chest, reducing the height by some inches; the chest itself becoming barrel shaped with a crumpled sternum. Irregular curvatures take place in the long bones with a tendency to fracture on slight injury. Due to rarefaction of the alveolar processes of the jaws the teeth may become loose.

Tetany is very common, but is not found in all cases. The spasms may last for hours, leaving numbness behind. Instability of gait is specially marked in pregnant cases, and, if properly treated, disappears before labour commences, so that it is not due to any physiological relaxation of the pelvic joints.

Excessive movements of the fœtus in pregnancy may be due to the disease, and fœtal rickets is now a proved occurrence in severe cases, with X-ray signs in the fœtus as early as the 35th week of intra-uterine life.

Rarer manifestations are a subcapsular cataract associated with the disease, formerly included under cataracta tetanica, though it may occur in osteomalacia cases which have not manifested tetany. The finger nails may become ridged, irregular, and tend to split.

The ovaries have been considered as the cause of the disease, but as it occurs in both men and women, and there is no histological difference between ovaries taken from active osteomalacia cases and ovaries removed from other cases, it is clear that they can be disregarded.

The parathyroids have been incriminated, and Erdheim was right when he pointed out the enlargement of the parathyroids in some cases of the disease, but this enlargement is a hyperplasia, a reaction to the disease, and clinically the administration of parathormone to osteomalacia cases makes them much worse.

Pathological changes (Histology).—Common to both rickets and osteomalacia are the following:

(1) Changes in the bone trabeculæ which are surrounded by broad osteoid seams.

(2) Changes in the costochondral junctions of the rib cartilages. "This is the only place where in the adult organism a cartilage-bone junction persists. Here in adult patients with osteomalacia the same proliferation of the cartilage is found as takes place in the epiphyseal discs of children with rickets" (Snapper, 1943).

Section of Physical Medicine

President—FRANK COOKSEY, O.B.E., M.D.

[*June* 18, 1947]

The Complex Behaviour of High-Frequency Currents in Simple Circuits

By P. BAUWENS, M.R.C.S., L.R.C.P.

ABSTRACT.—The fact that standing wave phenomena exist along transmission lines and loops conducting high-frequency electrical energy is responsible for effects of which therapeutic use can be made.

A. Power measurements are made possible because parallel transmission lines behave as power transformers of which the ratio varies with the length of these lines. In a generator designed by the G.E.C. the dimensions of the lines are such that after a preliminary estimation of the impedance of the load in the treatment field, the sensitivity of the meter can be adjusted so that the meter subsequently registers in watts the power absorbed in this load.

B. When using cable electrodes, in practice, the presence of strong electric fields between the antinodal portions of the loop as well as strong oscillating magnetic fields around the nodal portion gives rise to two distinct phenomena (fig. 6).

Search for currents resulting from the electric field on the one hand, and for eddy currents due to the magnetic field on the other, was carried out at St. Thomas's Hospital, in liquid phantoms by means of a probe (fig. 5*a*) incorporating a small lamp capable of being rotated in every direction. Voltage measurements were recorded by matching its light intensity with that of a similar lamp in circuit with a variable resistance and a voltmeter (fig. 5*b*).

When a portion of a cable electrode was coiled around a cylindrical vessel containing an electrolyte, the effects due to the two conditions could be dissociated. The following observations were made (fig. 7):

(*a*) By using the nodal portions of the loop only, it was shown that only eddy currents are produced and that the lower the resistance of the electrolyte the more easily they are produced. They are strongest at the periphery and rapidly fall off away from it, as shown by the curves of the graph in *fig.* 8.

(*b*) By using only the antinodal portions of the loop, coiled around the same vessel, coaxial or longitudinal currents can be demonstrated. It is interesting to note that these exist both at the periphery and at the centre.

(*c*) When the whole cable is wound around the vessel, the concentration of the electrolyte becomes the factor determining the way in which the energy will be dissipated: (1) with tap-water, it is found that no eddy currents can be demonstrated whereas coaxial currents exist; (2) with strong saline solutions the converse holds good; (3) with electrolytes of intermediate concentration both types of currents can be shown to coexist at the periphery while at the centre only coaxial currents can be demonstrated.

The fact that eddy currents and coaxial currents could be detected simultaneously and did not, as might be expected, give rise to a resultant, could only be explained by assuming that although eddy currents and coaxial currents coexisted as far as their effects on the pilot lamp were concerned, these two phenomena were not coincident as regards their phase relations. On examining the system more closely it became clear that the coaxial currents must be approximately 90 degrees out of phase with the eddy currents.

By means of another type of probe (fig. 5*c*) for surface work, consisting of two metallic buttons mounted on an insulating strip and bridged by a small lamp, P^3, similar to the one used throughout the investigations, it was possible to show that the same conditions existed in the body. It could be demonstrated that both coaxial and eddy currents occurred and that the predominance of one or the other type was dictated by conditions related to impedance. In the thigh just above the knee-joint, As to the long bones, bending may take place accompanied by the development of coxa vara; and fractures, often intraperiosteal, may occur.

The spinal column presents marked osteoporosis with marked bulging of the intervertebral discs into the vertebral bodies. There may be kyphosis with scoliosis, or a pure kyphosis, the latter being the rarer form.

The costochondral junctions of the ribs may show proliferation of the cartilage similar to that seen in the epiphyseal discs in early rickets.

Differential diagnosis.—Osteomalacia has to be distinguished from the other osteodystrophies; such as hyperparathyroidism; Paget's disease; renal osteodystrophy in adults; fragilitas ossium; senile osteoporosis; malignant metastases; and Hand-Schüller-Christian disease.

A difficulty is that osteomalacia may be superimposed on some of these diseases by virtue of the character of the invalidism which they have developed, involving confinement indoors, with lack of sunshine and a deficiency diet.

This may upset the calcium excretion so that even though in a hyperparathyroidism there may be hypercalcæmia there is a low calcium excretion. The majority of these affections are easily differentiated, but in the case of senile osteoporosis the matter is not so easy as administration of vitamin D may relieve the symptoms fairly quickly.

Speaking generally, however, taking into account the clinical symptoms and the chemical and radiological findings, the diagnosis of advanced osteomalacia is not difficult.

Where, however, one meets with a single case, in a region where osteomalacia is not common, there may be considerable difficulty in diagnosis.

It must be remembered that where there is one avitaminosis other vitamin shortages are almost sure to be present.

Treatment.—The result of treatment with any of the preparations of vitamin D has been very satisfactory. The provision of cheap calcium and vitamin-D tablets has transformed the position in North China.

The question of dosage and of the combination with it of other vitamins in the treatment of the disease is still unsettled.

One must remember that it is not merely in the well-marked case that treatment is important. Early symptoms of osteomalacia are not infrequently found in pregnant women, and there is no doubt of the benefit conferred on such women by regular dosage with calcium and vitamin D during the last six weeks of gestation.

It is not yet certain whether large single doses of vitamin D may be used as a prophylactic.

QUESTIONS NEEDING AN ANSWER

Two further points have yet to be defined: (1) The relation of the disease to hunger osteopathy. Pure starvation will cause an osteoporosis. Probably one will get a bone atrophy due to osteoblastic inactivity, where the special deficiency is not due to vitamin D alone; and (2) the relation of this disease to senile osteoporosis. In these latter cases the blood picture is normal and the crushing of the bodies of the vertebræ is the principal bone sign, but there is pain in the back and thighs and apparently arrest of the disease by treatment with vitamin D and calcium.

REFERENCES

HESS, A. F. (1929) Rickets Including Osteomalacia and Tetany. Philadelphia.
LIU *et al.* (1935) Calcium and Phosphorus Metabolism in Osteomalacia II. *Chinese Med. J.*, 49, 1.
MCCOLLUM, E. V., *et al.* (1922) *J. Biol. Chem.*, 53, 293.
MELLANBY, E. (1921) Experimental Rickets. Med. Res. Counc. Spec. Rep. No. 61, and (1925), No. 93.
POMMER, G. (1885) Untersuchungen über Osteomalacie und Rachitis. Leipzig.
RIBÉMONT-DESSAIGNES, A., and LEPAGE, G. (1894) Précis d'obstétrique. Paris, 931.
SNAPPER, I. (1943) Medical Clinics on Bone Diseases. New York.

References to osteomalacia in India may be found in the following papers:

GREEN-ARMYTAGE, V. B. (1928) *Ind. Med. Gaz.*, 63, No. 7.
MAXWELL, J. P., *et al.* (1930) *Proc. R. Soc. Med.*, 23, 639; (1935) 28, 265; (1939) 32, 287.
——, —— (1925) *J. Obstet. Gynæc.*, 32, 433.
WILSON, D. C., *et al.* (1929) *Ind. J. Med. Res.*, 17, 339; (1930) 17, 881, 903; (1931) 18, 951, 963, 969, 975.

In April 1935 I read before the Duchenne Society a short paper entitled "The Behaviour of Oscillating Currents in Complex Circuits". Since that time, I have become better acquainted with the behaviour of these currents and their vagaries. My greater respect for them has this time made me choose the less ambitious title of "The Complex Behaviour of High-Frequency Currents in Simple Circuits".

While the technical developments in the field of high frequency demanded by the exigencies of war have been considerable, their application to medicine has made but little progress.

One of the reasons for this discrepancy is that the medical man has an aversion to the mathematical way of expressing a phenomenon: while on the other hand the theoretical physicist, unfortunately, is only too well aware of the shortcomings of the non-mathematical conceptions of such phenomena.

The methods of producing high-frequency and ultra-high-frequency currents are now so numerous that the type of generator circuit employed in a particular machine is the radio engineer's problem. There are, however, in this respect two points with which the medical man may be concerned. The first relates to the abatement of radio interference. It is now moderately certain that legislation will come into being with a view to stopping incidental radiation from all types of equipment including electro-medical apparatus.

This will mean either working inside screened rooms or employing apparatus designed to work at frequencies allocated for free radiation. In order that apparatus should adhere strictly to the specified wave bands within the limits of tolerance imposed, it will have to be of very special design, probably crystal controlled.

My second point in this connexion takes me back to my lecture before the Duchenne Society, when, after demonstrating the existence of mechanical stresses in dielectrics subjected to alternating electric fields, I postulated that similar stresses might be produced in dielectrics subjected to high-frequency fields. I also propounded the hypothesis that such mechanical disturbances might provoke mild inflammatory reactions capable of eliciting defensive processes in living tissues.

At the same time it was realized that the dominant effect of high-frequency currents in the tissues was the production of heat with a consequent rise in temperature, which itself set a limit to the use of high-frequency currents at intensities sufficiently high to bring to light manifestations of another order.

It is not possible to predict what would happen if, instead of treating tissues by means of sustained high-frequency electrical energy, tissues were subjected to intermittent radio-frequency pulses of very high intensity separated by silent periods of sufficient length to allow for the dissipation of heat.

Those who have some technical knowledge of such matters will readily recognize an application of "Radar" technique in this.

It is disappointing to have to note that although this country was foremost in the field of Radar development, the only experimental work of this kind on biological materials was carried out by Dr. Johan Nyrop in Copenhagen, actually during, and after, the German occupation of Denmark.

The results of his investigations are epitomized in a letter published in *Nature* of January 12, 1946.

If the actual method of generating high-frequency currents is not of immediate interest or importance to the medical man using them, a knowledge of their behaviour in the circuit which includes the patient is essential, if they are to be used to their best advantage or if the need of measuring them arises.

One of the difficulties which appears to confront the non-technical mind is the recognition of an unfamiliar type of oscillating circuit.

Take a straight metal strip of say 1 metre in length and bend it so as to make it assume the shape of a gigantic hairpin. Few will recognize in this an oscillating circuit. Yet on closer examination the looped end may be regarded as a coil of only one half-turn and the open end as the plates of a condenser.

Thus we have inductance and capacitance which are the requisite factors for an oscillating circuit.

If brought within a short-wave field of approximately 2 m. wave-length this bent strip would become the seat of electrical oscillations of approximately 150 megacycles. This means that 150 million times per second, electrons pass from one prong of this system to the other and back again.

The presence of the electrons on one prong, and their deficiency on the other, creates an electric field across the open end of the system (C) while the to-and-fro movement of electrons in the loop (L) produces a magnetic field.

It must be realized for future reference that the electric field is strongest when no magnetic field exists and conversely.

in most cases both currents could be demonstrated. It could also be shown that when half the cable was wound clockwise and the other half anticlockwise, so as to cancel the magnetic field between the two halves, no eddy currents existed.

C. Present therapeutic applications of high-frequency currents involve the continuous dissipation of electrical energy in the load under treatment. Under these conditions the only detectable effect to which therapeutic value may be ascribed is the rise in temperature which results from heat production. This rise in temperature sets a limit to the power which can be used without risk of burns. Consequently effects other than thermal ones which might manifest themselves under higher intensities remain undetected.

It is not possible to predict what would happen if, instead of treating tissues by means of sustained high-frequency electrical energy, tissues were subjected to intermittent radio-frequency pulses of very high intensity separated by silent periods of sufficient length to allow for the dissipation of heat. Those who have some technical knowledge of such matters will readily recognize an application of "Radar" technique in this.

RÉSUMÉ—Les ondes électriques stationnaires avoisinant des conducteurs sièges de courants de haute fréquence, provoquent des effets qui doivent être pris en considération à la faveur de leurs applications thérapeutiques.

A. La mesure de l'énergie dissipée est rendue possible grâce au fait que des conducteurs parallèles se conduisent en transformateur. Dans une génératrice d'onde courte, mise au point par la G.E.C., les dimensions de ces conducteurs sont telles qu'après avoir préalablement établi l'impédance du sujet entre les électrodes condensatrices, la sensitivité de l'appareil de mesure peut être ajustée de façon à lire dès lors en watts l'énergie absorbée dans le sujet.

B. Avec l'emploi des électrodes inductrices la présence d'un puissant champ électrique entre les antinodes ainsi que d'un puissant champ magnétique oscillant, associé au node, donne lieu à deux phénomènes distincts (fig. 6).

À St. Thomas's Hospital on a recherché d'une part les courants de Foucault, et d'autre part les courants provoqués par le champ électrique. À cet effet on a fait usage d'une sonde munie d'une petite lampe électrique pouvant être orientée dans toutes les directions. Les voltages développés pouvaient être estimés par comparaison de l'intensité lumineuse émise par la petite ampoule, avec celle émise par une ampoule semblable en circuit avec une résistance variable et shuntée par un voltmètre (fig. 5*b*).

Avec une portion de l'électrode inductrice enroulée autour d'un vase cylindrique contenant une solution conductrice, les effets dûs au deux conditions existantes peuvent être séparés. Il est à noter que (fig. 7):

(*a*) en disposant la partie node de l'électrode inductrice autour du vase, seuls les courants de Foucault peuvent être décelés et que ceux-ci sont produits d'autant plus facilement que la résistance de la solution est faible. Ils sont d'ailleurs intenses à la périphérie et faiblissent rapidement en quittant celle-ci, ainsi que le démontre la courbe de la fig. 8.

(*b*) d'autre part, en n'usant que les antinodes de l'électrode inductrice enroulés autour du même vase, seuls les courants longitudinaux dûs au champ électrique se manifestent. Ceux-ci toutefois existent au centre du vase tout autant qu'à la périphérie.

(*c*) Lorsque l'électrode inductrice entière est enroulée autour du vase, c'est la concentration de la solution qui détermine la manière de laquelle l'énergie est dissipée: (1) Avec de l'eau du robinet, seuls des courants longitudinaux sont décelés tandis que les courants de Foucault sont faibles ou font défaut. (2) Avec une solution concentrée de sel marin, le contraire se manifeste. (3) Avec des concentrations intermédiaires, les deux courants peuvent coëxister à la périphérie tandis qu'au centre, seuls les courants longitudinaux se manifestent.

Le fait que les courants de Foucault et longitudinaux peuvent être décelés simultanément et sans donner lieu à une seule résultante ne peut être expliqué qu'en postulant que quoique ces deux courants coëxistent en tant que leurs effets sur la lampe exploratrice, ces deux phénomènes ne coïncident néanmoins pas quant à leurs phases. En effet, en examinant plus attentivement le circuit en question, il devient évident que ces courants doivent être déphasés d'environ 90°.

Au moyen de deux boutons métalliques montés sur un manche isolant et réunis par une petite ampoule (P^3 dans la fig. 5*c*) semblable à celles utilisées dans les expériences précédentes, il est possible de démontrer que les mêmes conditions existent dans le corps humain. Outre la présence de courants de Foucault et longitudinaux, on peut démontrer que la prédominance des uns ou des autres dépend de conditions ayant trait à l'impédance. Dans la cuisse, par exemple, on peut relever simultanément les deux courants. On peut aussi démontrer que les courants de Foucault peuvent être abolis en enroulant les deux moitiés du cable inducteur dans des directions opposées, de manière à neutraliser l'effet des champs magnétiques.

C. À présent les applications thérapeutiques de haute fréquence sous-entendent la dissipation continue de l'énergie électrique dans le sujet. Dans ces conditions, seuls les effets thermiques se manifestent. La hausse de température résultant de la production de la chaleur limite l'énergie utilisable sans crainte de brûlures. Par conséquent tout autre effet qui pourrait se manifester sous des intensités plus élevées reste caché.

Il est impossible de prévoir ce qui arriverait si au lieu de traiter les tissus à un régime de dissipation soutenue, on les soumettait à des trains d'ondes d'intensité très élevée séparés par des périodes inactives suffisamment longues pour permettre la dissipation de la chaleur dégagée. C'est une technique qui se rattacherait au "Radar".

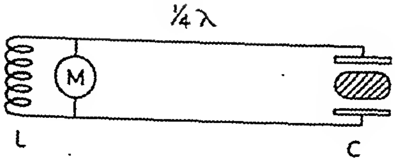


FIG. 1.

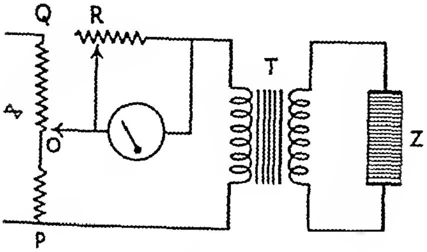


FIG. 2.

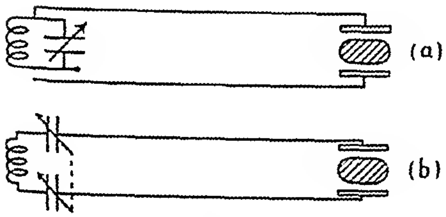


FIG. 3.

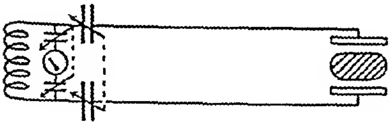


FIG. 4.

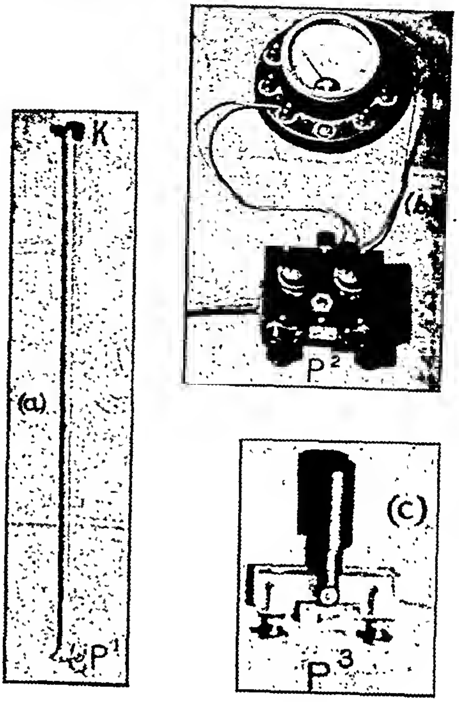


FIG. 5 *a*, *b*, *c*.

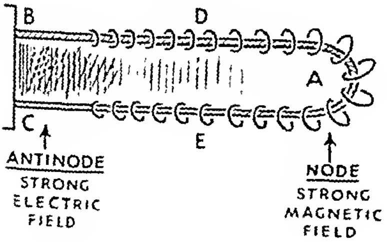


FIG. 6.

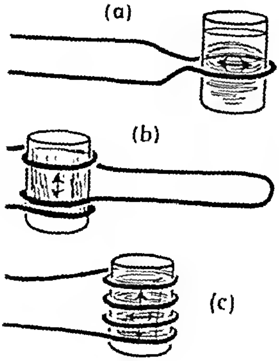


FIG. 7.

consisting of a single tuning condenser with the transmission lines and the patient's condenser field across it (fig. 3*a*) lend itself to the modifications required for power measurements by this method. Instead, a single oscillating circuit is used with the inductance, the transmission lines, the patient's condenser field and two ganged variable tuning condensers all in series (fig. 3*b*).

It is a circuit of this type, incorporating features designed to overcome the difficulties due to the complications mentioned, which has been adapted by the G.E.C. Laboratories for power measurement (fig. 4). One of its main points of interest is that the length of the transmission lines has been so adjusted that an automatic correction is effected for the power lost in the cables themselves. The sensitivity control in this instance is obtained by means of two small ganged condensers in series with the voltmeter.

The state of affairs just described exists in the patient's leads. On these transmission lines—when parallel—one can detect zones where a strong electric field exists and others where the magnetic field is strong. These conditions are referred to as standing waves and are in every way similar to the standing waves observable in analogous mechanical systems. Spectacular demonstration of this is afforded by Melde's experiment where a stretched string is attached at one end to the prong of a tuning fork and loaded at the other. Under the action of the vibrations the length of the string can be seen to break up into zones where practically no vibration occurs and zones where the amplitude of vibration is at its greatest. These zones are termed nodes and anti-nodes respectively.

That standing waves exist along transmission lines carrying high-frequency currents can equally well be demonstrated by means of a small loop of wire closed upon an ordinary light bulb in the case of voltage nodes and by means of a small neon tube in the case of anti-nodes.

An interesting feature of the standing wave phenomenon is that the voltage across one position of the parallel transmission line system bears a direct linear relation to the current in another.

If L and C (in fig. 1) represent the inductance and capacitance of an oscillating circuit in resonance with a high-frequency generator then, provided the transmission lines are $\frac{\lambda}{4}$ long, the voltage measured across the inductance L will vary directly with the current in the condenser C. So much so that a voltmeter M appropriately calibrated in amperes will give a direct reading of the current in the condenser field, that is, if the losses are negligible and the system is in resonance.

There is a definite relationship between the frequency of oscillation and the distance between the nodes and anti-nodes, the latter being equal to ¼ wave-length.

The direct consequence of this peculiarity is that transmission lines behave as power transformers which may in their effect be compared with an ordinary static transformer—provided the analogy is drawn with caution.

Imagine a transformer with an equal number of turns of wire on the primary and secondary windings. If an alternating current is fed into the primary, a current of substantially the same voltage and amperage will be available from the secondary. Should the number of turns of wire on the secondary be now progressively reduced it will be found that although substantially the same power is obtainable it will be of lower voltage but a higher amperage will be available. With, for instance, only one turn of wire on the secondary, enormous amperage and very low voltage will result, always provided the load is of the appropriate value.

With high frequencies it is important to note that whatever the length of the leads, the power supplied to the load via the leads has the same magnitude as the power fed into the leads, minus of course that proportion of the power which is lost in transmission. It is impossible to use at high frequencies the same type of power-measuring devices as are in common use at low frequencies. However, working in the G.E.C. Laboratories, Mr. Furneaux has developed a method of measuring the power supplied to the patient in short-wave diathermy. He makes use of a circuit which automatically combines a measurement of the resistance of the patient and of the current passing into him. The principles are best illustrated by outlining how the same circuit would measure power in a load subjected to A.C. at low frequency.

In fig. 2, T represents a transformer supplying power to a load Z. Its primary is supplied from a low-frequency source via the potentiometer QP. With this potentiometer set to the point O the E.M.F. has a definite value, say 10 volts. In series with the primary is a meter with a variable resistance R shunted across it. It will be appreciated that for a particular value of the shunt R the reading of the meter is a function of the current in the load, and as the power in the load is determined by the formula $W=I^2r$, then for a particular value of load resistance the meter could be calibrated directly in terms of the power into the load. But if now another load, having a different resistance, is connected to the secondary, this calibration will no longer apply. However, if the value of the shunt R is appropriately reset the meter calibration can be made to suit the changed load. Clearly what is needed is some means of measuring the resistance of the load so that the shunt R can be set to the correct value for each load. This can be achieved by setting the potentometer to the fixed point O, under which condition a predetermined E.M.F. is applied to the primary of the transformer, and the reading of the meter is a function of the resistance of the load. The meter reading under these conditions will therefore give the information which enables R to be set up to such a value that henceforth the meter correctly reads the power into the particular load under consideration.

In the case of high-frequency and ultra-high-frequency currents, the problem—although similar in its broad essentials—is complicated by the presence of standing waves and the losses due to absorption in the transmission lines. Nor does the customary output circuit

It has always been one of the drawbacks of short-wave therapy that it does not lend itself to being measured. The fact that one instrument can effect the measurement of current, or of the power dissipated must be considered an important step forward in dosimetry and will prove of invaluable assistance in technique of administration and prescription of short-wave therapy.

Other methods of computing power dissipated have been devised, notably by Mittelman, but they lack the simplicity of the one just described.

In this connexion I would, however, venture a cautionary remark to the effect that although these methods give information as to the total dissipation of energy, they give none as to where it is dissipated.

Take for example the treatment of a septic finger longitudinally and in series with the hand and forearm: the measurement of total power would in such a case not be as valuable as an assessment of the current in the finger.

From limited experience with the machine at my disposal it has already been abundantly clear that the measurement of both the current in amperes and of the power in watts must be available.

Before closing I should like to make some few remarks about that part of the output circuit more intimately concerned with the actual treatment.

Two principles are involved in the application of high-frequency currents to the patient. The first is based on the production of heat through power absorption in leaky dielectrics placed in a condenser field. The second depends on the production of heat resulting from the induction of eddy currents in tissues surrounded by a coil which is carrying a high-frequency current.

When the condenser method is used, only electric field phenomena need be considered and, provided the calculations of conditions in complex networks of impedances are regarded as a simple matter, the behaviour of the currents, as regards distribution and conversion into heat, are moderately straightforward.

In the case of treatments with the cable electrode, the problem becomes highly complicated on account of the difficulty of obtaining eddy currents only.

Experiments conducted at St. Thomas's Hospital have enabled us to come to some conclusions which I should like to put on record because they are of some practical importance and may, if noted, lead to improvements in technique with cable electrodes.

The search for the longitudinal or coaxial currents and for the eddy currents was carried out on liquid phantoms in a cylindrical vessel in collaboration with Dr. Waters and Mr. Styles. The probe used consisted of a glass tube having at one end a small electric bulb requiring a very low current and fitted with two small condenser plates (fig. 5*a*).

By turning knob K, this little lamp (P^1) could be made to rotate through 360 degrees in both the horizontal and vertical planes.

Accurate measurements of the E.M.F. impressed across the lamp (P^1) could be made by matching the light of a similar lamp (P^2) with a voltmeter across its filament and controlled by a variable resistance (fig. 5*b*).

Inasmuch as the cable electrode is a closed loop, it must have a nodal portion (A) where the current is high with a high magnetic flux and two antinodal portions (B and C) between which a strong electric field exists (fig. 6). Intermediate points (D and E) are in lesser degrees the seat of both magnetic and electrical phenomena.

When a portion of such a cable is coiled around a cylindrical vessel containing an electrolyte the effects of the two phenomena can be dissociated (fig. 7).

(*a*) By using the nodal portions of the loop only, it can be shown that only eddy currents are produced and that the lower the resistance of the electrolyte the more easily they are produced. Of course they are strongest at the periphery and rapidly fall off away from it, as shown by the curves of the graph in fig. 8.

(*b*) By using only the antinodal portions of the loop, coiled around the same vessel, coaxial or longitudinal currents can be demonstrated. It is interesting to note that these exist both at the periphery and at the centre.

(*c*) When the whole cable is wound round the vessel, the concentration of the electrolyte becomes the factor determining the way in which the energy will be dissipated: (1) with tap water, it is found that no eddy currents can be demonstrated whereas coaxial currents exist: (2) with strong saline solutions the converse holds good: (3) with electrolytes of intermediate concentration both types of currents can be shown to coexist at the periphery while at the centre only coaxial currents can be demonstrated.

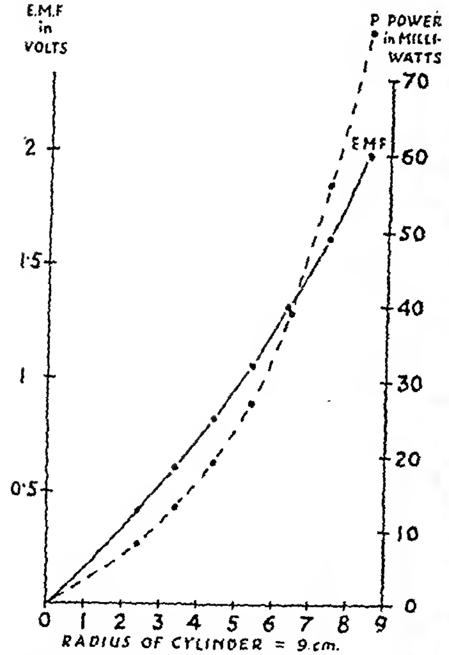


FIG. 8.—Full line curve (E.M.F.) shows the growth of the eddy current generating E.M.F. when the exploratory probe was moved from the centre to the periphery of the water phantom, along the 9 cm. radius. The broken line (P) shows the corresponding growth of the power measured in milliwatts.

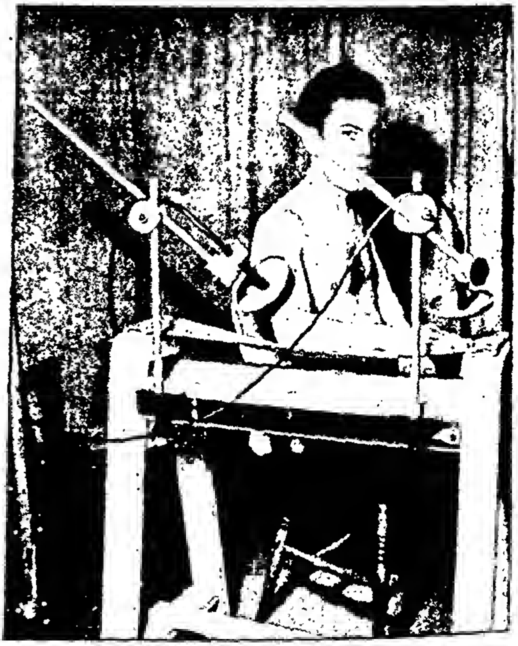


FIG. 9.

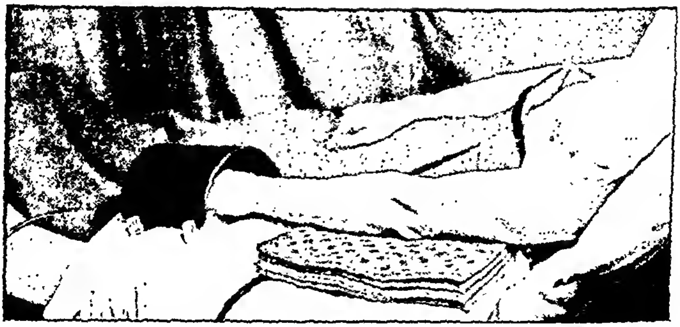


FIG. 10.

The operations involved are slightly more complicated and are as follows: The condenser electrodes are suitably placed and the generator is turned on to a definite pre-set but low output. With the sensitivity control of the meter at a standard setting the tuning condensers are then manipulated until the highest reading on the meter indicates that resonance exists. The meter now gives a measure of the resistance of the patient.

The pointer of the sensitivity control-knob is now made to point at a figure representing the resistance just noted. Once this is done, the meter registers on the power scale the watts dissipated in the patient and will continue to do so for any output of the generator provided the patient's circuit is kept in resonance. Many will have recognized that the steps taken to achieve this measurement are the same as those taken for measurements in the case of low-frequency currents.

Section of Pathology

President—A. B. Rosher, M.R.C.S., L.R.C.P., D.P.H.

(*October* 21, 1947)

Hæmophilus influenzæ and its Relation to Epidemic Influenza

PRESIDENT'S ADDRESS

By A. B. Rosher, M.R.C.S., L.R.C.P., D.P.H.

The majority of bacteriologists at one time or another have come under the spell of the Hæmophilus group. In this Pathological Section alone three former Presidents, namely, McIntosh, Fildes and Fleming, have all made valuable contributions to the literature of the subject and Dible, a former member of the Council, has also done likewise; furthermore Miles, a present member of the Council, has recently reviewed para-influenza bacilli in relation to endocarditis, and finally Edith Straker has provided some information as to the carrier rate of influenza bacilli in upper respiratory passages.

My interest in the group started seventeen years ago, when from 1929 to 1938 I set out to determine the carrier rate of influenza bacilli in the trachea of post-mortem subjects. I examined the best part of 1,000 strains at that time and since the war I have examined 100 or so more from various sources. When I chose the subject for an address, with this experience behind me, I thought I should have a comparatively easy task, but when I come to put my observations down on paper, I find it is not so easy as I imagined for now we have quite a large group to deal with and there are still many uncertainties to be cleared up.

In the olden days we had the respiratory type as described by Pfeiffer (1892, 1893), the Koch-Weeks bacillus which was considered identical with Pfeiffer's bacillus except for a tendency to cause conjunctivitis and, lastly, the somewhat rare strains known as para-influenza bacilli which synthesize the X factor and therefore only require V factor to be supplied in the ordinary culture medium to enable them to grow. Some comparatively rare strains of both influenza and para-influenza bacilli were known to be capable of forming a soluble hæmolysin.

This was the state of affairs until the year 1931 when two fresh observations were made on members of this group. Margaret Pittman, 1931, described a capsulated type of influenza bacillus possessing a specific soluble substance and since then she has identified six distinct serological types known as A, B, C, D, E, F, and it is of interest to note that the vast majority of cases of influenzal meningitis are due to one of these serological types, namely, type B.

Later in the year Shope described a bacillus which, in conjunction with a filtrable virus, gave rise to swine influenza. He called it *H. influenzæ suis* but pointed out that it was morphologically and culturally indistinguishable from other non-indole forming strains of *H. influenzæ*.

Table I.—Influenza Bacilli

H. influenzæ (Pfeiffer):	gives rise chiefly to infection of the respiratory tract; requires both X and V factors to be supplied for growth.
Koch-Weeks bacillus:	indistinguishable from the above but giving rise to conjunctivitis.
H. influenzæ suis:	indistinguishable from the above but giving rise to swine influenza in conjunction with a virus.
H. influenzæ (Pittman):	six serological types A, B, C, D, E and F. The type B is responsible for the vast majority of cases of influenzal meningitis.
Para-influenza bacilli:	differ from the above in synthesizing the X factor and therefore only requiring a supply of the V factor for growth. These organisms are sometimes found in connexion with infective endocarditis.
Hæmolytic influenza bacilli:	have been associated with respiratory disease but are rare in this country.
Hæmolytic para-influenza bacilli:	occasionally found in infective endocarditis.

The feature which at first appears puzzling is the fact that eddy and coaxial currents can be detected simultaneously and do not—as might be expected—give rise to a resultant. The small pilot lamp remains alight when rotated through 360 degrees. The only possible explanation is that although the eddy currents and the coaxial currents coexist as far as their effects on the pilot lamp are concerned, these two phenomena are not coincident as regards their phase relations. On examining the system more closely it becomes clear that the coaxial currents must be approximately 90 degrees out of phase with the eddy currents.

By means of another type of probe (fig. 5*c*) for surface work, consisting of two metallic buttons mounted on an insulating strip and bridged by a small lamp P^3 similar to the one used throughout these investigations, it is possible to show that the same conditions exist in the body. It can be demonstrated that both coaxial and eddy currents occur, and that the predominance of one or the other type is dictated by conditions related to impedance.

If the impedance is high, as for instance when the cable is wound around the whole length of an arm, the dissipation of energy in the form of coaxial currents appears to be favoured. If on the other hand the cable is wound around the trunk, the production of eddy currents appears to be favoured.

In the thigh just above the knee-joint, in most cases both currents can be demonstrated.

It can also be shown that when half the cable is wound clockwise and the other half anti-clockwise, so as to cancel the magnetic field between the two halves, no eddy currents exist.

The outcome of the more immediately practical aspects of some of our work is shown by the use of polythene-covered electrodes with turned-up edges and the method of clamping these electrodes to the treatment chair or limb rest (fig. 9).

Air-spaced tunnel electrodes also have their use when treating limbs or parts of limbs. They can be made out of ordinary rubber-covered electrodes held in a small wooden rack to keep them curved (fig. 10).

It will be noticed that a modification of this air-spaced tunnel electrode is used in conjunction with the machine incorporating the power-measuring instrument. Even in its prototype state this electrode has proved its adaptability to conditions.

My list of acknowledgments would be a long one if I mentioned by name everyone who had assisted me, for in addition to those directly associated with my work at St. Thomas's Hospital I am indebted to the Research Laboratories of the G.E.C. for their help, both from the point of view of technical advice and loan of apparatus. I would also mention Mr. Cox and his staff who took a lot of trouble in constructing the equipment I conceived.

strain there is a smallish circle surrounding the disc where no growth takes place (fig. 1).

If films are made from the periphery of this circle where there is obviously a struggle for existence the bizarre forms predominate, but about an inch away from this we find the coccobacillary or so-called typical forms predominating (figs. 2 and 3).

Some experiments are now being carried out by J. Fielding and myself to find out if it is a deficiency of V factor which causes this result. If this is the case penicillin probably has an antagonistic action on it. We have tried a few similar experiments with phenoxytol and streptomycin but have not been able to produce this effect with them. Therefore it looks as if the underlying principles of their antibiotic properties are different from those of penicillin.

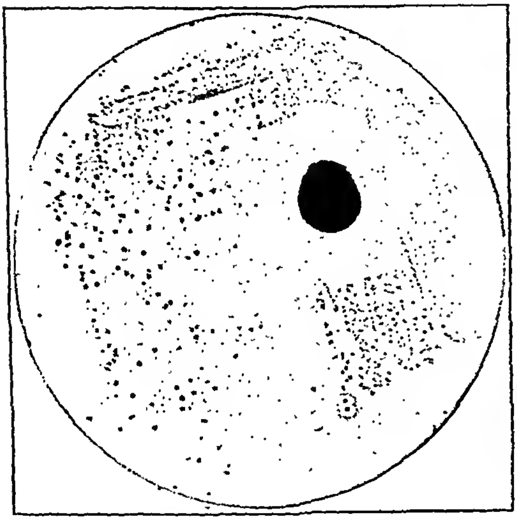


FIG. 1.—Fildes' medium inoculated with a penicillin-sensitive strain of *H. influenzæ*. The absorbent disc contains 10 units of penicillin. It is surrounded by a zone where the growth is inhibited.

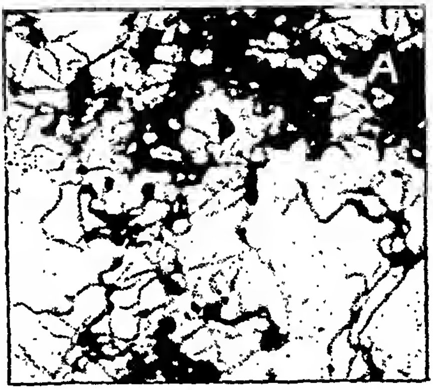


FIG. 2.—Film from periphery of inhibition zone (fig. 1 A) showing pleomorphic forms.

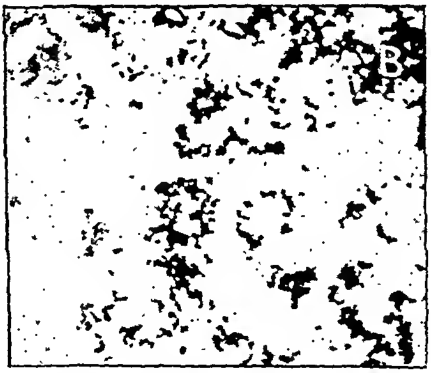


FIG. 3.—Film taken one inch from inhibition zone (fig. 1 B) showing coccobacillary forms.

The change of morphology is well marked in the case of Pittman rough and smooth colonies. Films from the rough colonies show the thread forms, &c., whereas those from the smooth show coccobacillary forms almost uniform in size. In older plate cultures, however, the bacteria from the smooth colonies also become pleomorphic and the bizarre forms are seen. The two morphological forms are interchangeable according to the nature of the food substance provided; they therefore can be regarded as environmental variants.

Table I shows a catalogue of the various members of the influenza group indicating their usual pathological propensities. However, overlapping frequently occurs and the Pfeiffer or respiratory strains may give rise to meningitis (Mulder, 1939, and Gordon *et al.*, 1944) and occasionally turn up in unexpected places, e.g. I have recently isolated a bacillus of the Pfeiffer type in pure culture from an intra-abdominal cyst and also a Bartholin's abscess. Then again Pittman strains may be found in the nasopharynx and this is, in all probability, the source of entry in meningeal infections.

In view of this probability I think no harm would be done from the public health point of view in swabbing the immediate contacts of cases of influenzal meningitis with a view to tracing possible sources of infection in this disease which, until recently, was almost always fatal.

The para-influenza bacilli are also found in unusual places (Stuart-Harris *et al.*, 1935) and I recently had one sent to me for identification from a case of ulcerative colitis. It has been suggested by Mulder (1947) that Pfeiffer's bacillus should be called *H. influenzæ bronchiale* and the Pittman B bacillus *H. influenzæ meningitidis*. If this suggestion were to meet with approval then some provision should be made, in our present state of knowledge, for the Koch-Wecks bacillus and it would probably have to be called *H. influenzæ conjunctivitidis*. The suggestion does not appeal to me in view of the diverse situations in the body where influenza bacilli may be found.

The hæmolytic influenza bacilli may be more common than we imagine, for Rivers (1919) and Lamont (1926) have shown that certain strains prefer rabbit's blood and will not grow well on sheep's blood agar, therefore some of them may be missed unless rabbit's blood is used. This also applies to the para-influenza bacilli for here again the somewhat elaborate technique required for their identification is not always carried out as a routine measure.

It is beyond the scope of this address to deal extensively with the vast literature which has accumulated regarding this fascinating group of organisms and I therefore propose to make a few observations on the morphological and cultural characteristics of strains that I have encountered and then pay attention to their pathogenicity in relation to epidemic influenza.

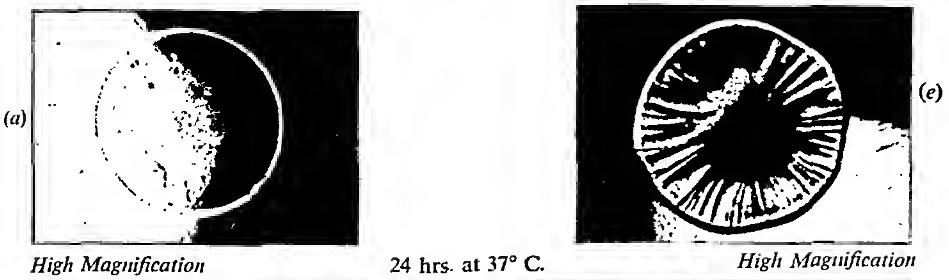
MORPHOLOGY

A considerable amount of confusion exists in the literature as regards the morphology of influenza bacilli. There is a tendency to regard the short and coccobacillary forms as *typical* and the longer bacillary, thread and globoid forms as *atypical*. In my opinion the so-called atypical forms occur when the organisms are growing under suboptimal conditions. This can be shown experimentally by inoculating a series of tubes containing broth and decreasing amounts of Fildes' solution containing the X and V growth factors, &c. In the tubes where there is an ample supply of the growth factors, films from the organisms show the coccobacillary or so-called typical forms to predominate but when one reaches about 1/10 or more below the normal supply there is a switch over to the bizarre forms which are normally called atypical.

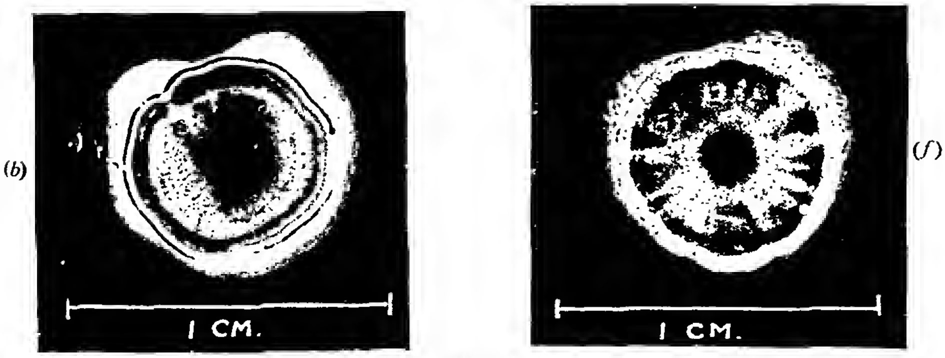
Further confirmation of this can be obtained by filming the large and small colonies of influenza bacilli near to a colony of staphylococcus where satellitism is seen. Films from the large colonies nearest to the staphylococcus where the food supply is good are coccobacillary, and films from the small colonies some distance away where the organisms are struggling for existence show the bizarre forms. I have reason to believe that the production of bizarre forms is due to insufficient supply of the so-called V factor rather than other factors.

This phenomenon is also well demonstrated on a plate of Fildes' medium with a small disc of absorbent, containing about 10 units of penicillin. If it is a sensitive

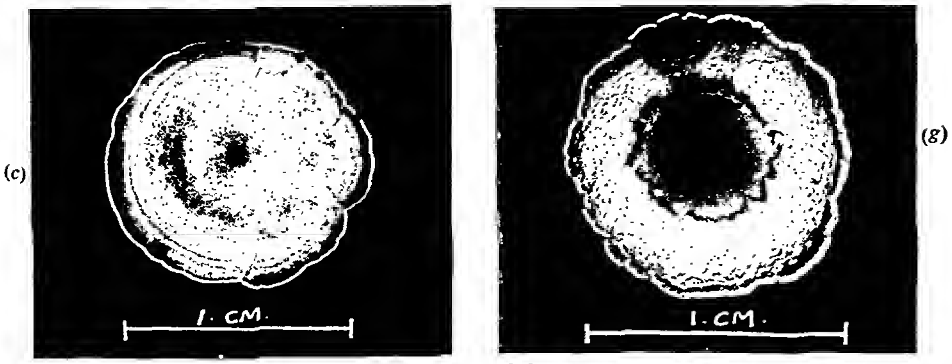
H. Influenzæ (Pfeiffer) *H. Influenzæ* (Pittman)


(a)
(e)
High Magnification
High Magnification

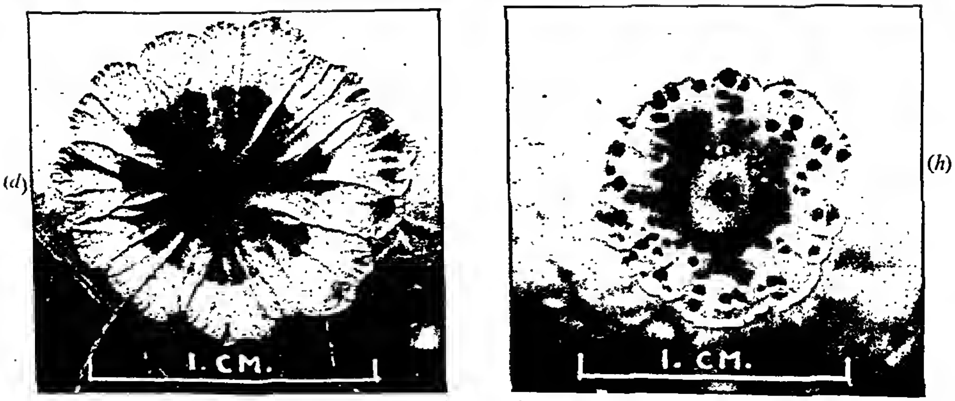
24 hrs. at 37° C.



3 days at 37° C.



1 week at 37° C.



3 weeks at 37° C.

FIG. 4.

Characteristics of Giant Colonies

Furthermore the bizarre forms are not infrequently found in mice after intraperitoneal inoculation; this again may be due to an insufficient supply of growth factors in that situation.

It seems to me that we have sufficient evidence to enable us to state *the only thing typical about the morphology of the influenza bacillus is its extreme pleomorphism and furthermore the pleomorphism can be produced at will if it is starved of its necessary food requirements.*

Certain strains are sometimes referred to as "atypical typicals" or "typical atypicals" when trying to describe their morphological appearances, but I think this nomenclature is absurd and it should be abandoned.

COLONIAL CHARACTERISTICS

In order to study the colonial characteristics of influenza bacilli in the present instance I have employed the method described by E. E. Atkin, 1923, for growing giant colonies of meningococci. By using double the ordinary quantity of culture medium in a Petri-dish and just pin-pointing out three or four inoculations on a plate and allowing the colonies to grow to maturity in six or seven days, he found colonial differences in the various types of meningococci and claimed to distinguish one serological type from another by this method. For the Hæmophilus group I have used Fildes' medium of the ordinary depth but have ringed the plate round with plasticine to prevent the medium becoming too dry.

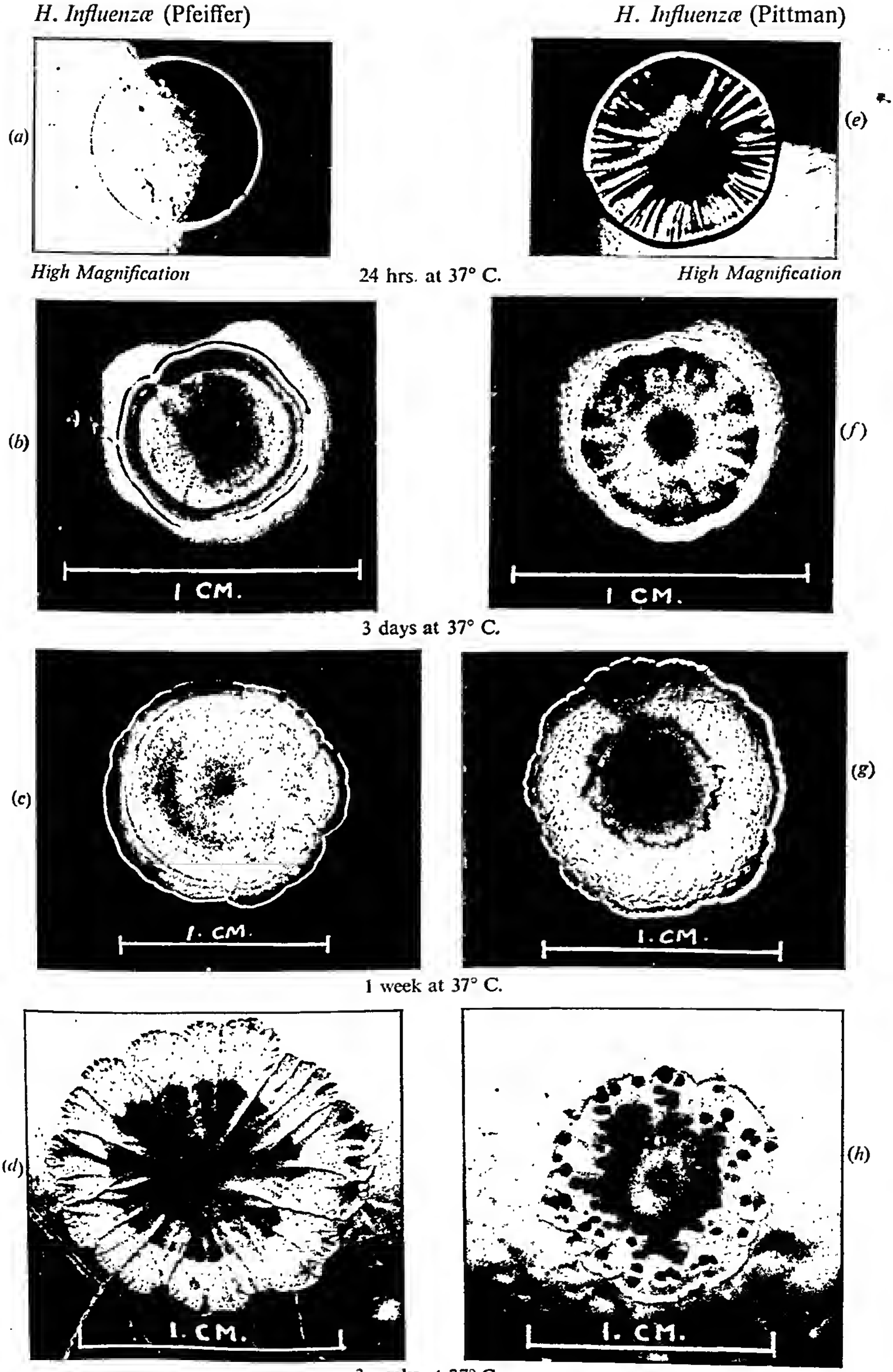
When the influenza bacillus is inoculated in this manner very large colonies are formed and after incubation at 37° C. for twenty-four hours the colony has already grown to about 3 mm. in diameter. At seven days it is about 8 mm. It usually reaches maturity in twenty-one days by which time it has become 1 cm. or more in diameter. The Pittman strains and Pfeiffer strains form entirely different and characteristic colonies when studied by this method. The differences can usually be detected even after twenty-four hours when viewed through a hand lens and by transmitted light. The characteristics are also seen quite well when the colonies are viewed from above with oblique lighting.

FIG. 4.—CHARACTERISTICS OF GIANT COLONIES

	H. influenzæ (Pfeiffer)	*H. influenzæ* (Pittman)
Twenty-four hours at 37° C.	(*a*) The colony is about 3 mm. in diameter. It has an entire edge and is finely granular throughout. It is not iridescent.	(*e*) The colony is about 3 mm. in diameter. It has an entire edge and fine striations are seen by transmitted light radiating out from the centre which is raised. They somewhat resemble the spokes of a wheel. The colonies are very iridescent.
Three days at 37° C.	(*b*) Increase in size to 6 or 7 mm. in diameter and the edge is becoming undulate. Fine granules are still present.	(*f*) Increase in size to about 6 or 7 mm. The edge is becoming undulate and the striations and the iridescence are still present and the latter is very well marked at the periphery.
One week at 37° C.	(*c*) Increase in size to about 8 or 9 mm. The colony is raised with a lobate convex bevelled edge.	(*g*) Increase in size to about 8 or 9 mm. The edge is now lobate and the colony resembles a sunflower when viewed by transmitted light with a hand lens. Iridescence and rays have disappeared.
Three weeks at 37° C.	(*d*) No marked increase in size, but great alteration in structure. The colony bears a striking resemblance to the head of a daisy when viewed by transmitted light.	(*h*) No marked increase in size but the "sunflower" appearance is still present and the colony is covered with knob-like excrescences.

At this point growth usually ceases and the colonies can be regarded as being mature. Why these knob-like excrescences should be formed with the Pittman colonies I do not know but I am further investigating the matter.

However I think it is wonderful that a small organism about 1μ in length can give rise to structures of such beauty and size when properly nourished.


H. Influenzæ (Pfeiffer)
H. Influenzæ (Pittman)
(a)
(e)
High Magnification
High Magnification
(b)
1 CM.
(f)
1 CM.
(c)
1. CM.
(g)
1. CM.
(d)
1. CM.
(h)
1. CM.

24 hrs. at 37° C.

3 days at 37° C.

1 week at 37° C.

3 weeks at 37° C.

FIG. 4.

Characteristics of Giant Colonies

Furthermore the bizarre forms are not infrequently found in mice after intraperitoneal inoculation; this again may be due to an insufficient supply of growth factors in that situation.

It seems to me that we have sufficient evidence to enable us to state *the only thing typical about the morphology of the influenza bacillus is its extreme pleomorphism and furthermore the pleomorphism can be produced at will if it is starved of its necessary food requirements.*

Certain strains are sometimes referred to as "atypical typicals" or "typical atypicals" when trying to describe their morphological appearances, but I think this nomenclature is absurd and it should be abandoned.

COLONIAL CHARACTERISTICS

In order to study the colonial characteristics of influenza bacilli in the present instance I have employed the method described by E. E. Atkin, 1923, for growing giant colonies of meningococci. By using double the ordinary quantity of culture medium in a Petri-dish and just pin-pointing out three or four inoculations on a plate and allowing the colonies to grow to maturity in six or seven days, he found colonial differences in the various types of meningococci and claimed to distinguish one serological type from another by this method. For the Hæmophilus group I have used Fildes' medium of the ordinary depth but have ringed the plate round with plasticine to prevent the medium becoming too dry.

When the influenza bacillus is inoculated in this manner very large colonies are formed and after incubation at 37° C. for twenty-four hours the colony has already grown to about 3 mm. in diameter. At seven days it is about 8 mm. It usually reaches maturity in twenty-one days by which time it has become 1 cm. or more in diameter. The Pittman strains and Pfeiffer strains form entirely different and characteristic colonies when studied by this method. The differences can usually be detected even after twenty-four hours when viewed through a hand lens and by transmitted light. The characteristics are also seen quite well when the colonies are viewed from above with oblique lighting.

FIG. 4.—CHARACTERISTICS OF GIANT COLONIES

	H. influenzæ (Pfeiffer)	*H. influenzæ* (Pittman)
Twenty-four hours at 37° C.	(*a*) The colony is about 3 mm. in diameter. It has an entire edge and is finely granular throughout. It is not iridescent.	(*e*) The colony is about 3 mm. in diameter. It has an entire edge and fine striations are seen by transmitted light radiating out from the centre which is raised. They somewhat resemble the spokes of a wheel. The colonies are very iridescent.
Three days at 37° C.	(*b*) Increase in size to 6 or 7 mm. in diameter and the edge is becoming undulate. Fine granules are still present.	(*f*) Increase in size to about 6 or 7 mm. The edge is becoming undulate and the striations and the iridescence are still present and the latter is very well marked at the periphery.
One week at 37° C.	(*c*) Increase in size to about 8 or 9 mm. The colony is raised with a lobate convex bevelled edge.	(*g*) Increase in size to about 8 or 9 mm. The edge is now lobate and the colony resembles a sunflower when viewed by transmitted light with a hand lens. Iridescence and rays have disappeared.
Three weeks at 37° C.	(*d*) No marked increase in size, but great alteration in structure. The colony bears a striking resemblance to the head of a daisy when viewed by transmitted light.	(*h*) No marked increase in size but the "sunflower" appearance is still present and the colony is covered with knob-like excrescences.

At this point growth usually ceases and the colonies can be regarded as being mature. Why these knob-like excrescences should be formed with the Pittman colonies I do not know but I am further investigating the matter.

However I think it is wonderful that a small organism about 1μ in length can give rise to structures of such beauty and size when properly nourished.

GROWTH REQUIREMENTS

For the sake of convenience I have referred to requirements for growth as the X and V growth factors. In the past this has been the custom but the work of Fildes (1921) has shown that the X factor is hæmin and more recently the Lwoffs (1937) have shown that the V factor originally described by Thjötta and Avery (1921) is cozymase.

PATHOGENICITY TO ANIMALS

Previous to 1931 *H. influenzæ* was regarded as being comparatively non-pathogenic to laboratory animals but in that year I showed (Rosher, 1931) that by incorporating a trace of Fildes' (1920) peptic digest containing the X and V growth factors in the inoculum, certain strains of the organism could be rendered highly pathogenic for mice by intraperitoneal inoculation giving rise to septicæmic death in sixteen to thirty-six hours. The following experiments have some bearing on the matter:

INOCULATION EXPERIMENTS

EXPERIMENT 1.—*Showing the Effect of Fildes' Solution on the Pathogenicity of Living Influenza Bacilli.*

A dose of 2,000 million organisms which had been washed three times in saline to remove any exotoxic substances was injected into the peritoneal cavity of ten mice. They all survived the injection.

Another batch of ten mice was injected with a similar dose of influenza bacilli but 0·05 ml. of Fildes' solution was added to each dose. They were all dead in thirty-six hours.

The most likely explanation of this result seemed to be the presence of the X and V growth factors in the digest. These factors are not normally present in the peritoneal cavity of a mouse and therefore growth does not take place, but when they are supplied with the inoculum the organisms can reproduce and give rise to a fatal septicæmia.

To gain further evidence as to the validity of this assumption it was decided to see how small a dose of living bacilli could be rendered pathogenic with the digest and a pathogenic strain was titrated down in a series of mice. The result of this was to show that the approximate lethal dose is somewhere in the region of 1,000 million to 2,000 million bacilli and when the dosage gets down to 500 million the reaction does not take place. This result led me to reconsider whether the stimulation by the digest was due to growth-promoting properties or to some other factor, for the comparatively large dose of 500 million bacilli should become lethal when facilities for reproduction are provided. I then tried to find out if the digest could enhance the virulence of dead influenza bacilli.

EXPERIMENT 2.—*Showing the Effect of Fildes' Solution on the Toxicity of Dead Influenza Bacilli.*

A dose of 10,000 million organisms killed by heating for half-hour at 60° C. and twice washed in saline was used. Ten mice were injected without Fildes' solution and all survived, whereas another ten mice were injected with the same dose plus 0·05 ml. of the solution and all died within two or three days. Skin tests on rabbits were then tried and the above results were confirmed.

EXPERIMENT 3.—*Showing the Effect of Injecting Influenza Bacilli with and without Fildes' Solution Intradermally into Rabbits.*

The results in Table II show that the difference in reaction between living and dead bacilli is negligible. Furthermore when a large dose of 1,600 million organisms is injected the stimulating effect of the digest is not seen as the organisms alone in that quantity produce a marked reaction. However with smaller doses such as 200 million, 100 million and 50 million the stimulation becomes apparent.

About 40 Pfeiffer or respiratory strains have been examined by this method, and I am impressed by its reliability, for, with only one exception, they gave typical colonies (fig. 4 *a*, *b*, *c*, *d*). At the commencement I did not examine them all to maturity but those I have since done have given very reliable results.

I have also examined a similar number of Pittman strains chiefly type B and they have invariably given satisfactory and characteristic results (fig. 4 *e*, *f*, *g*, *h*). I am now using Atkin's method for the study of other organisms and I hope to make a communication about this later.

It has previously been the custom to describe colonial characteristics on the appearance of overcrowded and of ill-nourished colonies after a brief residence of forty hours or so in the incubator long before they have reached maturity.

The morphology of a colony developing under optimal conditions is due to a blend of processes which are characteristic of the organism in any metabolic or antigenic state it may be in. This is not the case when colonies are growing under overcrowded conditions. In these circumstances the characteristic processes cannot function and impress distinct features on the colony. Thus crowded colonies cannot indicate properly the differences in characters—whatever they may be—of a Pfeiffer or a Pittman strain of *H. influenzæ*.

Pittman rough strains are now being tested in this manner for purposes of comparison with Pfeiffer respiratory strains as it has been suggested that they are identical; but as far as I have gone it looks as if they will have quite different appearances.

Several strains of *H. influenzæ suis* from the National Type Culture Collection have been tested in this manner and give colonies almost identical with the Pittman strains. I thereupon tested them with Pittman sera and found that they come down readily with Pittman B serum and Edith Straker kindly confirmed this result for me. The strains were sent from America and it is possible they have been wrongly labelled, if not it will be a matter of great interest if Shope's bacillus is a Pittman B strain. However, Shope is sending me some strains he can vouch for and I hope the matter will be cleared up shortly.

BIOCHEMICAL REACTIONS

Most observers have found that the fermentation of carbohydrates is not a very satisfactory method for differentiating the various members of this group and I have therefore never been tempted to try this method.

Nevertheless, I have used the test for indole production as a routine measure and on the whole I find it fairly consistent and reliable. Pittman, 1931, stated that types A and B were indole-positive both smooth and rough strains but Mulder, 1939, quotes her as saying that some strains of the B type are indole-negative. I have tested the strains in the National Type Culture Collection and find that types A, B, C, and F are indole formers but D and E are indole-negative.

I have also tested about 50 Pfeiffer strains isolated from pneumonic conditions and find them almost invariably indole-positive. I have also recently been trying the bile solubility test: Pittman 1931 stated that all of her strains both rough and smooth are bile-soluble. I get the same results with the National Type Culture Collection Pittman strains.

However, I have tested six recently isolated Pfeiffer or respiratory strains and they are not bile-soluble so this is evidence against Pfeiffer strains being rough variants of Pittman strains, which has been suggested.

inducting swine influenza, should not have borne a similar relationship to each other in their preceding host''. He continues:

''Certainly of all the horde of bacteria occurring in pandemic influenza it would be most peculiar to have a non-essential one chosen to accompany the virus in transferring to a new host.'' He sums up as follows: ''For these reasons I believe the infectious unit in pandemic influenza is composed of a specific complex of virus plus Pfeiffer's bacillus.''

This seems to be common sense and a matter of fundamental importance to be settled one way or another. If the disease is due to a *complex* a question to be decided is whether the bacillus is in the respiratory passages beforehand, and the soil therefore ripe for invasion by the virus, or are both virus and bacillus introduced together? If the former is the case then we should get some information of this by a study of the carrier rate of influenza bacilli before and during epidemics.

I can here offer a little suggestive evidence in favour of this hypothesis from the work I did from 1929 to 1938 (Rosher and Cole, 1939). When endeavouring to plot the incidence of influenza bacilli in the trachea of post-mortem subjects not suffering from respiratory disease, *I found a distinct seasonal trend in the carrier rate of this organism.* In the first quarter of the year, when influenza is usually prevalent, the carrier rate is highest whereas in the third quarter, when influenza is rare, it is lowest.

Straker (1939) who was working on the carrier rate in the nose and nasopharynx during a similar period found a seasonal trend to occur in the nasal cavities but to a less extent than in the trachea. The carrier rate in the nasopharynx was maintained at a steady level of about 60% to 65% irrespective of seasonal influences.

TABLE III.—PERCENTAGE INCIDENCE OF *H. influenzæ* IN CASES SHOWING NO EVIDENCE OF RESPIRATORY DISEASE

Quarter	Nasopharynx	Trachea	Nose
1st	66·9	39	9·8
2nd	64·7	23	8·0
3rd	60·5	19	3·8
4th	61·3	24	4·3

The reason for this seasonal extension into the nose and trachea remains to be determined but it undoubtedly happens at the time of year when influenza is likely to occur, whether in epidemic form or not.

At the moment I think we should concentrate on Shope's bacillus as being the most likely partner in the complex and try to determine if any specific differences can be found between this and the other indole-negative strains of influenza bacilli.

The study of giant colonies may give some help in the matter and an attempt to detect serological differences might be further explored. If these are successful then it would be well worth while to determine more accurately the carrier rate of these indole-negative strains in the nasopharynx, nose and trachea in epidemic and non-epidemic times.

During the period when the tracheal carrier investigation was being carried out there were seven years when I paid particular attention to the indole reaction and I have records of the carriers of indole-positive and negative influenza bacilli during that period.

I was trying to find out if there was any difference in the incidence of indole-positive and negative strains in epidemic compared to non-epidemic times. During this period, there were three years, 1931, 1933 and 1937, which might be regarded as epidemic years from the recorded deaths from influenza, but the other four years were normal. In the first quarter of the epidemic years there was a distinct increase in the carrier rate of indole-negative strains whereas the carrier rate of indole-positive strains remained fairly stationary.

TABLE II.—SHOWING AN EXPERIMENT TITRATING DOWN THE DOSAGE OF LIVING AND DEAD INFLUENZA BACILLI WITH AND WITHOUT FILDES' SOLUTION

Dose (millions/ml.)	Living – Fildes'	Living + Fildes' (0·02 ml.)	Dead – Fildes'	Dead + Fildes' (0·02 ml.)
1,600	++++	++++	++++	++++
200	+	++	±	++
100	+	++	0	++
50	0	++	0	++
20	0	0	0	0

Intradermal injection of 0·2 ml. (bulk) to a rabbit. The reactions were observed for four days and marked accordingly.

EXPERIMENT 4.—*To Try to Determine Which of the Individual Components of the Digest is Responsible for the Stimulative Effect.*

For this purpose the V factor was obtained from yeast extract, hæmin was used for the X factor and as Fildes' solution contains some pepsin, this was also tried.

The quantities used roughly correspond to the amount normally present in Fildes' solution and I am indebted to Jocelyn Patterson for carrying out their estimation.

A dose of 4,000 million dead bacilli was injected intraperitoneally into mice and as a result of this experiment there is a suggestion that: (1) Fildes' solution gives the best stimulation. (2) The X and V factors combined give nearly as much. (3) The X and V factors alone give slight stimulation. (4) Pepsin gives none at all.

The mode of action of Fildes' solution is therefore difficult to explain. The possibility of it being an additive toxic effect is not likely as 100 times the amount of the solution used for the tests can be injected into the peritoneal cavity of mice without harmful effects. The small amount of Fildes' solution used for skin tests gives rise to no reaction when injected by itself.

Alteration of permeability such as occurs with testicular extract was considered and experiments were carried out to test this possibility but the results were negative.

The enhancement of virulence also occurs when living or dead staphylococci are injected intradermally into rabbits and therefore it is not a specific reaction and the mode of action is obscure. *Nevertheless it is a useful method for comparing the pathogenicity of various strains of these and possibly other organisms.*

In 1937 L. D. Fothergill, T. H. Dingle and C. A. Chandler found that virulence of influenza bacilli for mice could be enhanced by suspending the organism in mucin.

Increase in mucin virulence of a strain of *H. influenzæ* by repeated passage through mice was shown and it was put forward as a useful method for passive immunization studies.

Here again, as far as I am aware, the mechanism is obscure.

PATHOGENICITY IN THE HUMAN SUBJECT IN RELATION TO EPIDEMIC INFLUENZA

When dealing with pathogenicity in the human subject the problem of major importance to be dealt with is whether organisms of this group play any part in bringing about epidemics and pandemics of influenza. Prior to the discovery of the virus by Smith, Andrewes and Laidlaw (1933) it was generally agreed that influenza bacilli often, but not invariably, play a part in the disease. The subject is dealt with in Kristensen's (1922) valuable monograph. Since then the extensive literature has been carefully reviewed by Topley and Wilson (1945) and allusion is made to the curious absence of these bacilli in certain epidemics particularly in the summer of 1918 which raised doubts as to their being the primary cause. However, I see no reason why all epidemics of so-called "influenza" should have an identical ætiology, and I doubt if our knowledge of viruses is sufficient to warrant this assumption at present. Furthermore it must be remembered that in 1918 the culture medium in use was distinctly poor for the isolation of these fastidious organisms.

Shope (1944) has expressed the opinion that the pandemic virus has a specific avidity for the Pfeiffer bacillus and with it constitutes the infectious unit. He states "if as seems likely the pandemic virus transferred from man to swine in 1918 and if as also seems likely the Pfeiffer bacillus transferred with it, it would be rather illogical to suppose that two agents bearing such an intimate relationship to each other in

I should therefore recommend the following measures to be adopted during an epidemic: Nasopharyngeal swabs should be taken and specimens of sputum and blood sent for examination. Inoculations should be made on plates of rabbit's blood agar and Fildes' medium.

Giant colonies should be studied and the indole reaction and other tests applied for accurate investigation of the strains. The patient's serum should be tested for antibodies against various strains of influenza bacilli including *H. influenzæ suis.* In addition, the carrier rate of the various organisms of this group in the nose, throat and trachea should be determined before and during epidemics, paying particular attention to indole-negative strains and, furthermore, any unusual frequency during epidemic times of other pathogens should be noted, as it is within the bounds of possibility that the virus might link up with other organisms on some occasions.

The recent work of Dubos *et al.*, 1947, has shown that the course of pulmonary tuberculosis in the mouse appears to be accelerated as a result of concurrent infection of the lung with influenza A virus and the effect is obtained with virus inocula sufficiently small to induce little or no definite viral pneumonia. There may be further examples of this dual action to be discovered. At any rate the work of Orticoni and Barbié on guinea-pigs should be repeated.

If the methods of investigation I have suggested were to be carried out I think in the course of a few years the problem of dual ætiology might be solved.

Apart from academic interest it is a matter of great importance as regards prophylaxis, and possibly treatment. Already prophylactic vaccines of virus are on trial and if the disease is due to a partnership the question arises as to whether the bacillus should be included.

Shope finds that *H. influenzæ suis* vaccines alone give a certain amount of protection against swine influenza but the protection afforded by the virus vaccine alone is so good that he does not consider it worth incorporating a bacillary antigen as well.

However; it is not certain that the same would hold good in man. As regards treatment. the question of an antiserum would arise for already evidence is accumulating (Zinnemann, 1946) as to the value of antiserum in conjunction with antibiotics in meningitis due to Pittman B strains, so if this organism or another influenza bacillus was to be incriminated an antiserum might have some value in combating severe infections of respiratory influenza in times of epidemic.

Dr. H. C. Engbaek of the State Serum Institute in Copenhagen told me recently that he cured 17 out of 19 cases of influenzal meningitis by this method, which is most encouraging.

This brings me to the end of my remarks on the influenza group. At the moment it is a subject which, perhaps, is a little in the background as we have been spared another pandemic such as occurred in 1919 and proved to be more deadly than war. However, nobody can prophesy when a pandemic will occur again and we must be prepared for such an eventuality.

I hope these suggestions may be of some use in the future when dealing with epidemic influenza.

SUMMARY

(1) Some evidence is brought forward to show that the pleomorphism of *H. influenzæ* occurs when the organism is growing under suboptimal conditions. It is suggested that this may be due to an insufficient supply of the V factor.

(2) The bizarre forms also occur when penicillin comes into contact with the organism and therefore if the above suggestion is correct penicillin may have an antagonistic action on the V factor.

It will be noticed in Table IV that in the epidemic years the carrier rate of indole-positive strains was 18% compared to 22% in the non-epidemic years whereas the carrier rate of indole-negative strains was 26% as against 13%, representing +13% ±4·0 in favour of the epidemic years and *it must be remembered once again that Shope's bacillus is indole-negative.*

TABLE IV.—INCIDENCE OF INDOLE + AND − STRAINS OF *H. influenzæ* IN THE TRACHEA IN CASES SHOWING NO EVIDENCE OF RESPIRATORY DISEASE DURING THE FIRST QUARTER OF THREE EPIDEMIC AND FOUR NON-EPIDEMIC YEARS

	Epidemic years	Non-epidemic years	Diff. and S.E.
Indole + ..	18% (34/189)	22% (43/196)	−4±4·1
Indole − ..	26% (50/189)	13% (25/196)	+13±4·0

Let us assume that these indole-negative strains correspond to Shope's bacillus, then in the epidemic years there was an average of 26% of people not suffering from respiratory disease but carrying this organism in the trachea and therefore suitable subjects and soil for the reception of the virus, for, as Shope says, "the virus has specific avidity for the influenza bacillus and with it constitutes the infectious unit".

It must be remembered that these figures only represent the people who are carrying the indole-negative strains in the trachea and their frequency might be greater if these strains were looked for in the upper respiratory passages.

In my experience the Pfeiffer or so-called respiratory strains are usually indole-positive and from the figures I have shown their carrier rate does not alter appreciably in the epidemic years, whereas carriers of indole-negative strains certainly seem to increase.

It is a rather short run of years on which to base conclusions, but the result is sufficiently suggestive to warrant further investigation on these lines, the frequency of other pathogens in epidemic and non-epidemic times should also be plotted to act as a control.

As long ago as 1919 S. F. Dudley, in dealing with the subject of carriers, stated: "Perhaps this harmless organism (*B. influenzæ*) especially favours the spread of a filter passer which, though extremely virulent in its presence, cannot gain a footing in the human organism without the help of Pfeiffer's bacillus." He continues: "Since the above paragraph was first written A. Orticoni and Barbié have reported that *B. influenzæ* and filtered sputum from an influenza case are harmless to guinea-pigs separately, but together are extremely pathogenic." He concluded as follows: "Should this observation be confirmed it would go a long way towards proving the double ætiology of influenza as due to a filter passer plus Pfeiffer's bacillus."

This observation was made in 1919 and I wonder if the experiment has ever been repeated, if not, in my opinion, it is high time that it was.

W. J. Wilson *et al.* in 1924 reported the presence of agglutinins for the influenza bacillus in almost 100% of cases during the acute pyrexial period in the outbreaks of influenza in Ulster in 1922 and 1924.

Sometimes they were found as early as the first day of disease and in convalescence as a rule they rapidly disappeared. In a large number of control sera the vast majority gave negative results. In 1946 C. H. Andrewes kindly sent me a few sera to test from patients suffering from influenza and the results were of sufficient interest to warrant further investigation.

Section of Otology

President—H. V. Forster, M.C., M.B., Ch.B., M.Sc.

[*February* 7, 1947]

Transmeatal Attico-Antrotomy in Chronic Tympanomastoid Suppuration

By A. Tumarkin, F.R.C.S.Ed.

Introduction.—Ten years ago I became convinced that radical mastoidectomy could not give me the results I wanted. Seeing a reference to the work of Thies on the transmeatal route (Thies, 1912; Trampnau, 1935–36) I decided to investigate its possibilities. This paper gives an account of the technique I finally evolved and of the results.

Technique.—The operation is performed under general anæsthesia and the site of the incision is infiltrated with weak adrenaline solution. The incision starts at Shrapnell's membrane and ascends the outer attic wall to the roof of the external auditory canal (fig. 1). It then traverses the roof in the mid-line. At the junction of the osseous and cartilaginous canals it turns downwards and outwards. This marks out an elliptical flap which is easily elevated. The incision is made with a fine knife via a slotted aural speculum and it is easy, using one edge of the slot, to catch the flap and roll it into the floor of the meatus. A little hæmorrhage occurs and is easily controlled by pressure of the speculum. When it is mopped or sucked away, the whole bone of the outer attic wall and post-superior wall is clearly seen. This approach sacrifices no skin and is confined strictly to the osseous canal.

The bone removal should always commence at the tympanic ring. Fine labyrinth gouges 2 to 3 mm. in width are used to excise semilunes of bone as in fig. 2. This is the "mauvais pas" of the operation because the facial nerve is in the direct line of the gouge. It is, however, a good sixth of an inch away and, with reasonable care, it need never be damaged. The bone at the tympanic annulus is very thin and can be cut away with the gentlest of hammer blows. The aditus and the short process of the incus, the facial nerve, and the stapes come into view almost at once, giving perfect orientation. The cavity is extended by progressively flaking semilunes of bone from the cut margin. It is tempting—especially in deep narrow ears—to try and enter the antrum at a more superficial point T (fig. 2), but that is a very grave mistake for the following reasons: First, it is much more difficult to cut a hole than to flake off an edge of bone, and the operator is easily disorientated (incidentally, the dental drill has no place in this operation). Also, if the antrum is successfully entered at T there still remains the "bridge" between it and the annulus which has ultimately to be removed under the added disadvantage that it tends to be obscured by blood seeping down from the cut bone above it. By the flaking method the surgeon always has a clear view of the dry edge of bone which he has to remove.

It is useless to attempt this operation with punches. A punch delicate enough to permit of use under direct vision could not bite the bone away. A more powerful punch completely blocks the view and, being used blind, is dangerous; dislocation of the incus is almost certain to occur. The same objections apply to attempts to "protect" the facial nerve by passing a Stacke director into the aditus. This obscures the field, dislocates the incus and may indeed bruise the nerve. The only satisfactory method is to use sharp gouges as described above.

(3) Attention is drawn to the value of the giant colony method for differentiating organisms which are closely allied.

(4) The importance of the indole reaction and bile solubility test is emphasized for differentiating these organisms.

(5) A method is put forward for the study of the pathogenicity and toxicity of various strains of influenza bacilli for laboratory animals.

(6) Some literature is reviewed on the ætiology of epidemic influenza in relation to it possibly being due to a complex of virus plus influenza bacillus.

(7) Some experimental evidence is produced in favour of this theory.

(8) Some suggestions are made for investigations to be carried out before and during epidemics, the result of which might decide the question of dual ætiology.

In conclusion I wish to thank those who have helped me with this work, namely Sir Paul Fildes, O.B.E., F.R.S., and Professor G. S. Wilson, K.H.P., for criticisms, Professor A. Bradford-Hill for help with the statistics, Professor H. S. Barnard and Dr. A. B. Bratton and others for tracheal swabs. Mr. W. E. Crawley, Mr. W. F. Cole and Miss V. A. L. Brews for technical assistance, Mr. J. E. Andrews for the photographs and finally Miss S. Goldstein for clerical assistance.

REFERENCES

Atkin, E. E. (1923) *Brit. J. exp. Path.*, **4**, 325.
Dubos, R. J., *et al.* (1947) *J. exp. Med.*, **86**, 203.
Dudley, S. F. (1919) *Lancet* (ii), 476.
Fildes, P. (1920) *Brit. J. exp. Path.*, **1**, 129.
——, (1921) *Brit J. exp. Path.*, **2**, 16.
Fothergill, L. D., Dingle, J. H., and Chandler, C. A. (1937) *J. exp. Med.*, **65**, 721.
Gordon, J., Woodcock, H., and Zinnemann, K. (1944) *Brit. med. J.* (i), 779.
Kristensen, M. (1922) Investigation into the Occurrence and Classification of Hæmoglobinophilic Bacteria. Copenhagen.
Lamont, J. A. (1926) *Canad. med. Ass. J.*, **16**, 1447.
Lwoff, A., and Lwoff, M. (1937*a*) *Proc. roy. Soc. B.*, **122**, 352, 360.
——, —— (1937*b*) *Ann. Inst. Pasteur*, **59**, 129.
——, —— (1937*c*) *C. R. Acad. Sci., Paris*, **204**, 1510.
Mulder, J. (1939) *J. Path. Bact.*, **48**, 175.
—— (1947) 4th International Congress for Microbiology. Abstracts of Communications.
Pfeiffer, R. (1892) *Dtsch. med. Wschr.*, **18**, 28.
—— (1893) *Z. Hyg. InfectKr.*, **13**, 357.
Pittman, M. (1931) *J. exp. Med.*, **53**, 471.
Orticoni, A., Barbié, L., and Augé (1919) *Pr. méd.*, **27**, 247.
Rivers, T. M. (1919) *Johns Hopk. Hosp. Bull.*, **30**, 129.
Rosher, A. B. (1931) *Brit. J. exp. Path.*, **12**, 133.
——, and Cole, W. T. (1939) *Rep. publ. Hlth. med. Subj., Lond.*, No. 90.
Shope, R. E. (1931) *J. exp. Med.*, **54**, 349, 373.
—— (1944) *Medicine, Baltimore*, **23**, 415.
Smith, W., Andrewes, C. H., and Laidlaw, P. P. (1933) *Lancet* (ii), 66.
——, ——, —— (1935) *Brit. J. exp. Path.*, **16**, 291.
Straker, E., Hill, A. B., and Lovell, R. (1939) *Rep. publ. Hlth. med. Subj., Lond.*, No. 90.
Stuart-Harris, C. H., Wells, A. Q., Rosher, A. B., Mackie, F. P., and Wilson, G. S. (1935) *J. Path. Bact.*, **41**, 407.
Thjötta, T., and Avery, O. T. (1921) *J. exp. Med.*, **34**, 97, 455.
Topley, W. W. C., and Wilson, G. S. (1946) Principles of Bacteriology and Immunology, 3rd Ed. revised by G. S. Wilson and A. A. Miles. London.
Wilson, W. J., Dunn, J. H., and Blair, E. M. M'V. (1924) *J. Path. Bact.*, **27**, 336.
Zinnemann, K. (1946) *Brit. med. J.* (ii), 931.

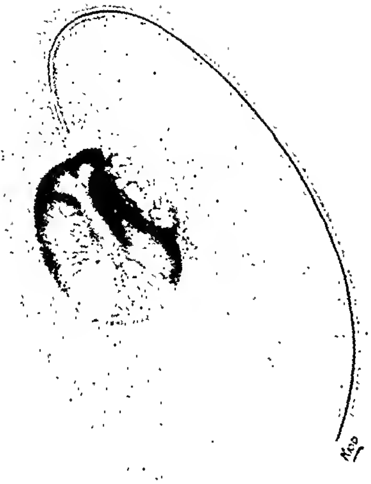


FIG. 1.—Transmeatal attico-antrotomy. The incision. Note the granulations on the post-superior quadrant of the tympanic ring. The tympanic membrane in that region has collapsed on to the inner tympanic wall.

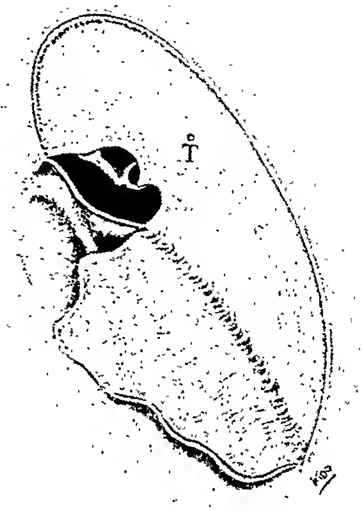


FIG. 2.—Transmeatal attico-antrotomy. The "mauvais pas". The flap has been elevated and is now thrust into the floor of the external auditory canal. The first two semilunes of bone have been chipped away, carrying the granulations with them. The long process of the incus comes into view and the crura of the stapes. The antrum could be reached by plunging a dental drill through the post-superior meatal wall at T. This is not recommended (*see* text).

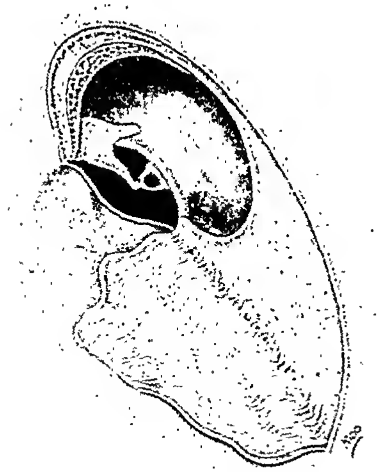


FIG. 3.—Transmeatal attico-antrotomy. The bone excision completed. Showing incus, semicircular canal, facial nerve and stapes. This shows a comparatively limited excision of bone. The exposure can easily be extended forwards, upwards or backwards. The strip of bone overlying the head of the malleus would normally be removed so as to gain access to Prussak's pouch.

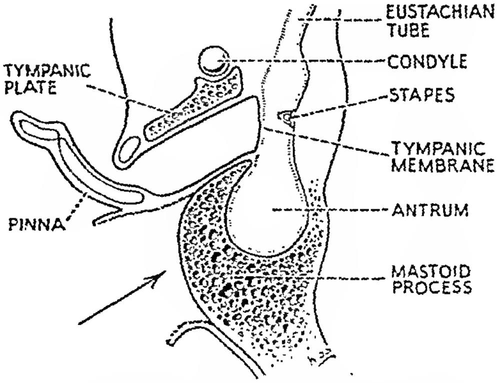


FIG. 4.—Classical radical mastoidectomy. Showing post-auricular incision and radical excision of mastoid process (shown by shaded area).

It might appear at first sight that three hands are needed: one to hold the retractor, one to hold the gouge and a third to hold the hammer. That apparently has been the practice on the Continent. Thies entrusted the hammer to his assistant—a laborious and precarious technique. Heermann constructed special self-retaining retractors so that he could do the hammering himself. The most valuable retractor is a slotted speculum. A set should be available rising in half millimetres from 4 to 8 mm. The largest possible speculum should be used so that the pressure is maintained on the cut flaps, thus ensuring hæmostasis.

The extent of the operation is determined by the findings. If necessary, the whole mastoid process can be explored by excising the intervening bone. The anterior pouch of the attic should be left till the last, when the surgeon is well orientated and has adequate space to manœuvre. The bone in that region is commonly rather thick but is readily removed by the same technique of progressively flaking off the cut margin. Thus the incudo-malleolar articulation is exposed and the decision finally made as to the fate of the incus (fig. 3). The ossicle is often submerged in granulations, but providing the incudo-stapedial articulation is intact it is justifiable to retain it. These cases commonly recover with excellent hearing. Even if suppuration persists, it is easy at a subsequent operation to pick out the diseased ossicle. The fate of the malleus depends on the incus. There is nothing to be gained functionally by leaving the malleus by itself, but the attached drum helps to protect the inner wall of the tympanum. Even so it is advisable to amputate the head of the malleus which is prone to necrosis.

The operation cavity is carefully irrigated and examined for loose spicules of bone and granulation tissue. Then the skin flap is rolled into place. It laps over the facial ridge and covers the raw edges right up to the semicircular canal. This is a most important feature of the operation (fig. 6). The functional results of mastoid surgery are greatly influenced by the rapidity with which epithelialization and healing of the aditus occur. In radical mastoidectomy, the surgeon is careful to sling the flap with sutures externally, but pays little attention to the state of affairs deep in. Consequently the aditus and facial ridge are only too often permanently covered with granulations. In attico-antrotomy the flap is gently smeared into position and then Zelex penicillin is squirted in (*see* page 771). No sutures or ligatures of any kind are necessary.

The first dressing is done about a week later and consists merely of syringing the Zelex out. The whole after-treatment is painless, a most important feature, especially when dealing with children. Nothing more than the simplest of aural toilets is necessary. In some cases the ear is dry within three weeks. Frequently, however, small granulations form in the roof at the site of the original incision. If neglected, these grow downwards and obstruct the atticostomy. They do not adhere to the facial ridge because the latter is protected by the skin flap. The granulations should be gently snared off under cocaine anæsthesia, after which the cavity usually heals rapidly. In general, one may confidently expect a healed cavity within four to six weeks. In those cases which prove resistant the trouble is usually in the tympanum and not in the mastoid cavity.

Rationale.—This underlines the rationale of atticotomy. In chronic otorrhœa the disease is in the middle ear, attic and aditus.The stress which has been laid on the idea of disease ramifying throughout the mastoid process has distorted the picture. Despite the exhortations of many authorities it is common practice to exenterate the mastoid process in search of outlying disease. Lempert (1938*a*), for instance, specifically states that a radical mastoidectomy should start with a complete exenteration of the process exactly as in a cortical mastoidectomy. We must condemn this attitude. From the practical point of view, it is shown to be unjustifiable by the fact that the limited excision of attico-antrotomy will produce better results by far. As to the theoretical point of view, let us remember that in the great majority of these cases there are no outlying cells—diseased or otherwise. The process is

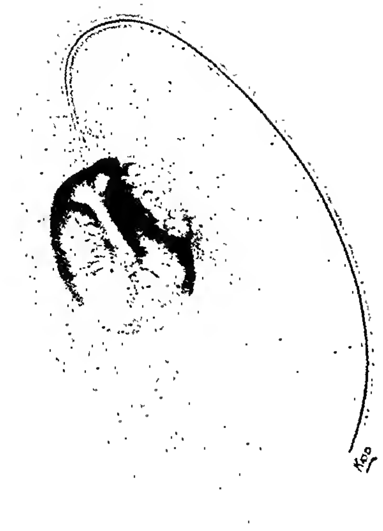


FIG. 1.—Transmeatal attico-antrotomy. The incision. Note the granulations on the post-superior quadrant of the tympanic ring. The tympanic membrane in that region has collapsed on to the inner tympanic wall.

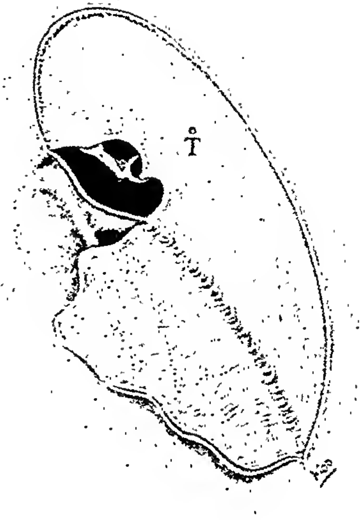


FIG. 2.—Transmeatal attico-antrotomy. The "mauvais pas". The flap has been elevated and is now thrust into the floor of the external auditory canal. The first two semilunes of bone have been chipped away, carrying the granulations with them. The long process of the incus comes into view and the crura of the stapes. The antrum could be reached by plunging a dental drill through the post-superior meatal wall at T. This is not recommended (*see* text).

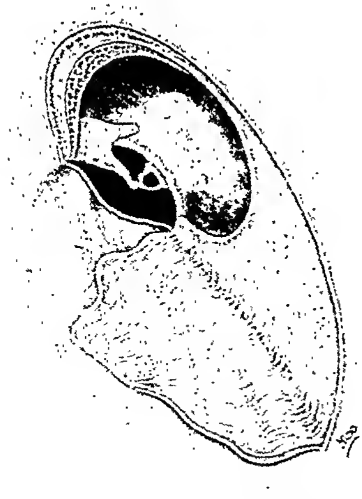


FIG. 3.—Transmeatal attico-antrotomy. The bone excision completed. Showing incus, semicircular canal, facial nerve and stapes. This shows a comparatively limited excision of bone. The exposure can easily be extended forwards, upwards or backwards. The strip of bone overlying the head of the malleus would normally be removed so as to gain access to Prussak's pouch.

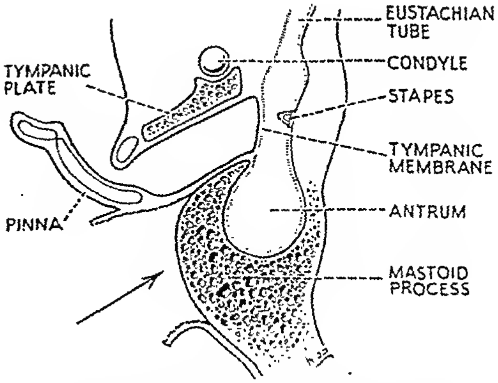


FIG. 4.—Classical radical mastoidectomy. Showing post-auricular incision and radical excision of mastoid process (shown by shaded area).

hypoplastic and is of the ivory or diploetic type. Again chronic middle-ear suppuration is a very benign condition. In 60% to 80% of cases it yields to simple hygiene of the outer ear. We deduce that in those cases there can be little or no involvement of bone, and that the disease must be confined to the accessible soft tissue adjacent to the tympanic ring. In the remaining intractable cases, why must we fly to the opposite extreme of very radical surgery? Surely there must be intermediate stages between the benign condition which we cure by simple hygiene and this desperate condition which demands complete mastoidectomy. Those intermediate stages will consist of a little caries of the tympanic ring—or of the ossicles and perhaps some accumulation of granulation and debris in the aditus or antrum. It follows that the operation of choice will *commence* at the tympanic ring and not *finish* there. In this way the main focus of the disease is immediately exposed and the surgeon can be guided by his findings. If the appearance suggests more extensive disease there is no difficulty whatsoever in following it up.

It seems to me that the heroic quality of the classical transmastoid approach (fig. 4) has crept in because of our obsession with the intracranial complications. These loom too largely in our minds and in our textbooks. Whatever may have been the case in the past, to-day they are interesting rarities. I will concede readily that where such complications are suspected, the widest possible exposure is necessary and can only be provided by extensive circum-aural incisions. But these cases are rare, and they will become even rarer if we begin to pay attention to the functional significance of chronic otorrhœa. I am the last person to advocate indiscriminate surgery. Nevertheless I submit that any suppurating ear which has resisted conservative treatment should be explored by the transmeatal route without delay. In that way we could abolish the group of intracranial complications which is caused by neglected chronic suppuration. More than that, we could give our patients some prospect of retaining, if not improving, their hearing. Is it an exaggeration to say that we are reluctant to do a radical mastoidectomy if hearing is good. We fear to make it worse. We prefer our patient to be deaf so that we can operate with impunity. Even if otorrhœa persists after the operation and deafness is as bad, or worse, we can claim to have saved him from the dreaded intracranial infections. The following extract expounds that viewpoint:—

> *Objects sought in operation.*—There are two principal reasons why the radical mastoid operation should be done: First, for the relief of an annoying and at times offensive otorrhœa; and second, the prevention of intracranial complications, which are always serious. This does not mean that the radical operation should be resorted to in all cases of chronic suppurative otitis media which do not wholly recover under conservative methods of treatment. Every case of chronic otorrhœa does not present the same degree of potentially serious complications and each must be dealt with on its own merits. When the suppuration continues as the result of carious erosion or a necrotic process, intracranial complications are threatened, but on the other hand, if the disease is confined to the mucosal lining of the tympanum, it is quite unlikely that intracranial complications will arise, thus contra-indicating a radical operation.—JACKSON, C., and COATES, G. M., 1929, The Nose, Throat and Ear and Their Diseases, pp. 537-8, London.

The writer of that article is led to the conclusion that mere persistence of discharge is not necessarily an indication for operation. That is an attitude which I most strongly oppose. Persistent otorrhœa *is* an indication for exploration of the attic and antrum. I will except the occasional cases of eustachian infection which resist treatment. They are rarities. Most eustachian infections are readily controlled by hygiene—ionization and attention to the nasopharynx. The vast majority of intractable cases have a post-superior or a Shrapnell perforation. In them pus is seeping over the floor of the aditus, filling Prussak's pouches and eroding the incus. If we think of such cases from a point of view of function, we shall regard them with the same urgency as the oculist regards chronic glaucoma.

Our aim must be to save the incus. It is generally held that the functional results of radical mastoidectomy are not improved by preservation of the incus, and that otorrhœa may persist if a diseased ossicle is retained. Those are the penalties we pay for the delayed operations. The position is quite different in atticotomy. I now have a number of patients on whom I have been able to preserve a functioning incus and in every case the hearing is excellent. This is particularly important in the children of the poorer classes, amongst whom bilateral middle-ear suppuration is so common.

How are we supposed to treat these cases? MacCuen Smith advises as follows:

> "It not infrequently happens that young children suffer from a bilateral chronic otorrhœa which resists persistently all non-operative measures for relief. It has been my custom with these children to perform first a simple mastoid operation on the ear in which the hearing is more impaired, on the theory that the principal pathology is located in the mastoid antrum and this procedure corrects the otorrhœa in a fair number of instances. If the disease is not eradicated by this means, then a modified radical mastoid operation, which completely exposes the antrum, should be tried. This failing, we should seriously consider the advisability of performing the radical mastoid operation, selecting the worse ear first and noting the effect on the hearing, and should still further postpone additional operative measures if audition has been seriously impaired unless further complications threaten."—S. MacCuen Smith: Jackson and Coates, The Nose, Throat and Ear and their Diseases, p. 542.

It is not difficult to detect an undertone of defeat in these recommendations, and the reasons are not far to seek. If the primary disease is in the aditus and attic, then exenteration of the mastoid process can do no good at all. This fallacious idea underlies Heath's operation and also Bárány's operation of mastoidectomy without a meatal plastic. Both these procedures are uniformly disappointing.

During the past year, I have operated on thirty-five school children. In no case was there the slightest complication. Nearly all of them left the hospital within a week and in most cases the ear was dry within a month to six weeks. Unfortunately these children are still not discovered soon enough—or the operation is postponed too long in the hope that conservative treatment may ultimately succeed. There is no real difficulty in recognizing the ear which is not doing well. It continues to seep a little foul pus—or it heals and then breaks down again. These cases should always be explored promptly.

Criticisms.—In the past this operation has been subjected to fierce criticisms. We may list them as follows: (1) Performed in the dark in a pool of blood. (2) Insufficient room for manipulation. (3) Danger to vital structures—stapes; facial nerve; dura and lateral sinus. (4) Cannot with certainty reach limits of disease.

(1) The operation is performed in the brilliant light of a bull's eye reflected by a head mirror down a large aural speculum. Hæmorrhage is reduced to a minimum—first because the incision is a minute one and secondly because the soft tissues are firmly compressed by the aural speculum. Thus, no blood seeps from above down to obscure the point of attack. A little blood may well up from the depths but is easily absorbed by a pledget of wool. By flaking the bone from below upwards (i.e. from within outwards) one keeps the point of attack well in sight all the time. It is always above the tide mark of the blood. It is of course necessary periodically to irrigate and suck out blood and pus so as to clarify the situation but I have never had to cut short any operation because the field was obscured with blood.

(2) It is true that the approach is constricted. The skin flap is perhaps half as big as a postage stamp and instruments have to be correspondingly delicate. The operation is admittedly difficult and demands meticulous care and precision.

(3) The danger to vital structures looms too largely in the imagination of the theoretical critic. Thies, Jnr., declares that his father operated on 1,500 cases without a death and with very few major complications. I have myself performed over 300 attico-antrotomies without a single death. In 3 cases I have caused a transient facial palsy (i.e. subsiding within two weeks); in one case a labyrinthitis supervened which was cured by penicillin. I have never injured the lateral sinus and although I have frequently exposed the dura of the middle fossa, I have never torn it or set up any intracranial complications.

(4) This criticism loses its force when we recall the pathological conceptions on which the operation is founded. In these cases we are dealing with localized disease

hypoplastic and is of the ivory or diploetic type. Again chronic middle-ear suppuration is a very benign condition. In 60% to 80% of cases it yields to simple hygiene of the outer ear. We deduce that in those cases there can be little or no involvement of bone, and that the disease must be confined to the accessible soft tissue adjacent to the tympanic ring. In the remaining intractable cases, why must we fly to the opposite extreme of very radical surgery? Surely there must be intermediate stages between the benign condition which we cure by simple hygiene and this desperate condition which demands complete mastoidectomy. Those intermediate stages will consist of a little caries of the tympanic ring—or of the ossicles and perhaps some accumulation of granulation and debris in the aditus or antrum. It follows that the operation of choice will *commence* at the tympanic ring and not *finish* there. In this way the main focus of the disease is immediately exposed and the surgeon can be guided by his findings. If the appearance suggests more extensive disease there is no difficulty whatsoever in following it up.

It seems to me that the heroic quality of the classical transmastoid approach (fig. 4) has crept in because of our obsession with the intracranial complications. These loom too largely in our minds and in our textbooks. Whatever may have been the case in the past, to-day they are interesting rarities. I will concede readily that where such complications are suspected, the widest possible exposure is necessary and can only be provided by extensive circum-aural incisions. But these cases are rare, and they will become even rarer if we begin to pay attention to the functional significance of chronic otorrhœa. I am the last person to advocate indiscriminate surgery. Nevertheless I submit that any suppurating ear which has resisted conservative treatment should be explored by the transmeatal route without delay. In that way we could abolish the group of intracranial complications which is caused by neglected chronic suppuration. More than that, we could give our patients some prospect of retaining, if not improving, their hearing. Is it an exaggeration to say that we are reluctant to do a radical mastoidectomy if hearing is good. We fear to make it worse. We prefer our patient to be deaf so that we can operate with impunity. Even if otorrhœa persists after the operation and deafness is as bad, or worse, we can claim to have saved him from the dreaded intracranial infections. The following extract expounds that viewpoint:—

> *Objects sought in operation.*—There are two principal reasons why the radical mastoid operation should be done: First, for the relief of an annoying and at times offensive otorrhœa; and second, the prevention of intracranial complications, which are always serious. This does not mean that the radical operation should be resorted to in all cases of chronic suppurative otitis media which do not wholly recover under conservative methods of treatment. Every case of chronic otorrhœa does not present the same degree of potentially serious complications and each must be dealt with on its own merits. When the suppuration continues as the result of carious erosion or a necrotic process, intracranial complications are threatened, but on the other hand, if the disease is confined to the mucosal lining of the tympanum, it is quite unlikely that intracranial complications will arise, thus contra-indicating a radical operation.—JACKSON, C., and COATES, G. M., 1929, The Nose, Throat and Ear and Their Diseases, pp. 537-8, London.

The writer of that article is led to the conclusion that mere persistence of discharge is not necessarily an indication for operation. That is an attitude which I most strongly oppose. Persistent otorrhœa *is* an indication for exploration of the attic and antrum. I will except the occasional cases of eustachian infection which resist treatment. They are rarities. Most eustachian infections are readily controlled by hygiene—ionization and attention to the nasopharynx. The vast majority of intractable cases have a post-superior or a Shrapnell perforation. In them pus is seeping over the floor of the aditus, filling Prussak's pouches and eroding the incus. If we think of such cases from a point of view of function, we shall regard them with the same urgency as the oculist regards chronic glaucoma.

Our aim must be to save the incus. It is generally held that the functional results of radical mastoidectomy are not improved by preservation of the incus, and that otorrhœa may persist if a diseased ossicle is retained. Those are the penalties we pay sloughing and post-aural fistulation, collapse of the pinna and so on. None of these complications ever occurs in atticotomy. Again the post-operative dressings and after-care of a mastoidectomy do still entail much pain and misery. After atticotomy there is practically no pain or discomfort. Healing is achieved much more rapidly and the discharge is never copious or offensive. The functional results of attico-antrotomy are in my opinion unquestionably superior to those of the radical operation. This I attribute to the following factors:

(1) Preservation, where possible, of the incus.

(2) Accurate positioning of skin flaps over the aditus floor. This prevents formation of granulations at that point and promotes rapid epithelialization of the cavity.

(3) Minimal excision of bone and minimal displacement of soft tissues. The radical operation leaves a comparatively large cavity which has to fill secondarily with granulations. These then contract down and are more or less covered with skin. It is agreed that one of the most important factors in preservation of function is the promotion of rapid healing. The atticotomy cavity has practically no raw area to heal, with the exception of the anterior edge of the incision to which I have already referred. Healing time is thus reduced to less than half of the time required by mastoidectomy with correspondingly good effect on hearing.

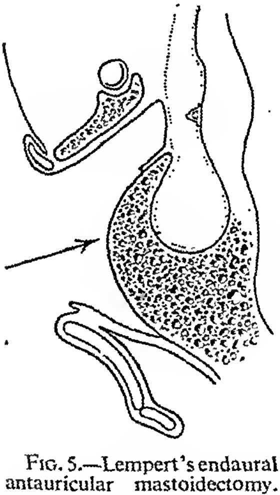


Fig. 5.—Lempert's endaural antauricular mastoidectomy. Showing endaural excision of skin, mobilization of concha and radical excision of bone as in fig. 4.

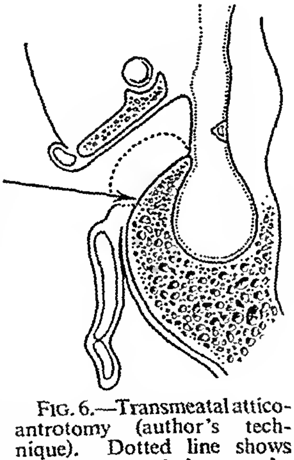


Fig. 6.—Transmeatal attico-antrotomy (author's technique). Dotted line shows skin flap turned downwards. Note limited excision of bone (shown by shaded area).

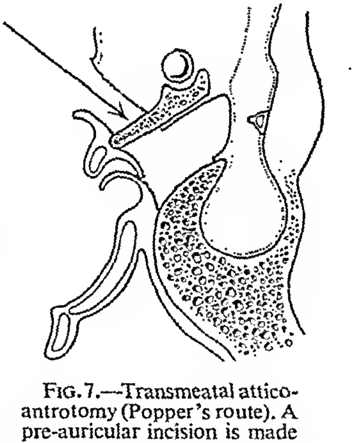


Fig. 7.—Transmeatal attico-antrotomy (Popper's route). A pre-auricular incision is made so as to expose the tympanic plate. This is excised and the external auditory canal is entered through its anterior wall. Bone excision as in fig. 6.

(4) In mastoidectomy the surgeon burrows from the surface downwards forming a conical cavity. The functioning tissues are reached towards the end of the operation, lying deep in the apex of the cone and liable to be obscured by blood seeping down from all sides. In the technique I have described the ossicles and aditus are exposed immediately and examined. The surgeon is always above the blood and cutting away from it rather than delving into it. He is thus able to preserve the functioning structures under direct vision all the time.

(5) The mastoidectomy cavity—even when apparently quite dry—can be a source of recurring trouble to the patient. Sometimes it is so widely open that draughts of cold air can set up caloric effects on the labyrinth. The wax-bearing area is displaced into the cavity and so waxy crusts are liable to accumulate. The lining membrane is of poor vitality and is readily ulcerated by this mass. By contrast the atticotomy flap does not encroach on the wax-bearing area, so that crusts do not accumulate. The

in attic and aditus. The antrum is usually involved in that its lining is unhealthy. Outlying cells are few and the whole tract recovers rapidly when it is adequately drained. It should not be thought that this limits attico-antrotomy to a small proportion of cases. Leaving out the rare cases in which intracranial complications are suspected the transmeatal route is applicable to at least 90% of all cases. The real refutation of these criticisms lies in the results. It is impossible to brush aside the statistics quoted by Thies, and an analysis of my own cases shows that the transmeatal operation can yield results which are in every way superior to the classical operation.

Advantages.—The intrinsic merits of the operation emerge when we compare it with alternative techniques. Although Shambaugh finds it identical with ossiculectomy the very names indicate the fundamental difference between ossiculectomy and atticotomy. In ossiculectomy the surgeon assumes the middle-ear structures are useless and proceeds to ablate them. In atticotomy the stress is on function. The surgeon is out to preserve. He explores the attic and antrum being guided entirely by the pathological findings. It is said that the end-result is the same, but this is incorrect. It is true that in atticotomy the incus frequently must be sacrificed. The fault lies not in the operation, but in the fact that we do it too late. The following account of ossiculectomy is extracted from Jackson and Coates' textbook:

> Ossiculectomy may be done under local anæsthesia but is quite painful. Membrana tympani circumcised from ring—cut away from malleus, and removed.
>
> TO EXTRACT MALLEUS
>
> (1) *American method.*—Insert angled tenotome behind malleus and scrape it down—thus dividing ligaments and tensor tympani. Body of bone seized by Sexton's upward grasping forceps and delivered. Traction on handle alone is usually disastrous resulting in fracture.
>
> (2) Delstanche-Brunschwig upward-cutting ring curette is slipped up the manubrium, &c., &c.
>
> REMOVAL OF INCUS
>
> A choice of methods: It may disappear altogether unless preliminary disarticulation from stapes has been done. *Continental School* uses right and left incus hooks. American operators prefer opposite rotation of the incus hook. Accidents are not infrequent. Sustained pressure by hook may damage facial nerve. Too strong backward pressure may lose ossicle in aditus, antrum, attic pouch, hypotympanum or eustachian tube mouth. Successful in 40% to 60%. Merits wider study and eventual employment of younger surgeons of special deftness.

One must be struck by the multiplicity of manœuvres described, the variety of instruments necessary to perform them and the many disasters which are liable to attend them. The removal of the malleus under direct vision during a radical operation commonly requires considerable force and it must be difficult, dangerous and painful to scrape it from under cover of the outer attic wall. This blind groping can surely not be compared with the simple precision of atticotomy in which the ossicles are clearly exposed and examined before disposal. Nor is ossiculectomy likely to succeed unless the carious annulus is removed and the aditus drained. Efforts are indeed made to utilize an attic punch for that purpose, but as I have already pointed out the bone punch is futile and dangerous in that situation. In brief, ossiculectomy abandons the ossicles without a struggle. In this it is too radical. On the other hand it is too conservative in dealing with the disease. It cannot be extended at will. Any effort to use punches merely scrapes away the skin of the attic wall.

The issue between attico-antrotomy and the various transmastoid operations has already been touched on but the main difference may be usefully summarized. First, although attico-antrotomy is perhaps the more difficult operation—it is from the patient's point of view much smaller in every way. It takes from twenty to forty minutes. No sutures or ligatures are *ever* used and the manipulation of the soft tissues is reduced to a minimum. With the advent of sulphonamides and penicillin the post-operative complications of mastoidectomy have become rare, nevertheless they do still occur. We may note hæmorrhage, stitch abscess, perichondritis, secondary

A thorough familiarity with the transmeatal technique is invaluable in dealing with many other conditions also. Despite injunctions to the contrary I have had no difficulty in removing osteomata of the osseous canal. Secondary ossiculectomy (when a previous conservative mastoidectomy or atticotomy has failed) is performed with the utmost ease and I have converted many Heath operations into radicals by the same technique. In the past I have also performed attico-antrotomy on a few cases of cortical mastoidectomy in which suppuration had persisted. It is noteworthy that Lempert's latest operation of tympanic sympathectomy is transmeatal and I believe with Popper (1946*b*) that functional surgery of the ear will in the future be more and more associated with this route.

Results.—In an effort to assess the value of atticotomy, a questionnaire was sent to fifty consecutive cases:

Forty-two replies were received, yielding the following figures:

All age-groups were represented from 5 to 65

Duration of disease	
Under one year	1
1 to 3 years	13
3 to 20 years	14
Over twenty years	14

Average stay in hospital after operation 7 days

Post-operative pain	
None	28
Slight	13
Severe	1

It is clear that we are very far from our ideal of "early operation".

Healing

The cases were then examined to check the condition of the cavity:

Completely dry tympanomastoid cleft	29	38 healed operation cavities
Dry mastoid cavity but slight discharge from middle ear	9	
Slight discharge from mastoid as well as middle ear	4	

In no case was there any gross purulent discharge.

Healing time	
1 to 3 weeks	14
3 to 6 weeks	11
6 to 12 weeks	2
Over 12 weeks	2

Effect on hearing	
Improved	21
Unaltered	19
Worsened	2

These figures were analysed as follows by the Department of Applied Mathematics, Liverpool University (Professor L. Rosenhead).

With data of this nature it is convenient to calculate two limits within which the true proportion (e.g. of moist mastoid cavities) may be expected to lie. More precisely, we give below an upper and lower limit such that, if the experiment were repeated many times under the same conditions and these limits calculated in the same way each time, then the true proportion would lie between these limits in 95% of cases, outside in only 5%.

We find: (1) *Mastoid cavity*. Proportion "moist" almost certain to lie between 2% and 24% (and therefore "dry" between 76% and 98%).

(2) *Middle-ear cavity*. Proportion "moist" almost certain to lie between 17% and 48% (and therefore "dry" between 52% and 83%).

(3) *Hearing*. With a probability of being correct lying between 92·5% and 97·5% we may assert that the proportion "improved" lies between 20% and 67%. "Unaffected" between 15% and 62%, while the proportion "impaired" is less than 18%.—(R. L. Plackett, 24.4.47.)

The following conclusions may justifiably be drawn from these figures:

(1) Since 38 operation cavities out of 42 healed completely and since the remaining four do not produce any gross purulent discharge, attico-antrotomy is quite adequate for dealing with the disease in the mastoid process. The fear of leaving outlying disease is without foundation.

(2) When healing occurs it does so far more rapidly than after a radical operation. The figures quoted are the patients' estimates and no doubt some reported a dry ear in the absence of overt discharge when in fact epithelialization was not quite complete. Several in fact reported a dry ear after the first dressing. Even allowing for this exaggeration it is clear that, in successful cases, healing takes place with gratifying rapidity. In six cases the patient was discharged as cured after the fourth dressing.

tiny cavity is lined by tough healthy skin and is tucked deep in out of harm's way. In favourable cases the patient is completely free of any further symptoms.

The endaural antauricular approach.—Many of my colleagues seem to confuse the approach described by Lempert (fig. 5) with the true transmeatal approach. Actually a comparison of the two techniques reveals that there is no resemblance whatsoever between them. Lempert (1938*b*) indeed specifically states in describing his approach:

> The endaural antauricular operation on the temporal bone is not performed through the external auditory canal, but through a widely-opened mobile window, which, together with the auricle, may be displaced in every direction over the temporal bone.

The differences may be summarized as follows:

(1) Lempert forms a window by excising a triangle in the soft tissues of the outer half of the canal.
The true transmeatal approach sacrifices no skin and is limited to the osseous canal.
(2) Lempert starts by plunging a dental drill down into the antrum.
In my opinion the dental drill is a bad instrument, especially when suppuration is present. This leaves the bridge to be dealt with later on. I have already discussed the disadvantage of this procedure.
(3) Above all, however, Lempert prescribes a radical excision of the whole mastoid process.

His operation is essentially a transcortical mastoidectomy. It only differs from the classical operation in that he approaches the cortex in front of the concha instead of behind it.

The following extract from his description shows how radical Lempert's endaural mastoidectomy is:

> The surgeon must expose tegmen, zygoma, base of the petrous—the sinus plate and the fallopian canal. He must venture posterior to the entire course of the lateral sinus and burrow down to the tip of the mastoid infero-anterior to the lower curve of the lateral sinus. He must expose the tympanic orifice of the eustachian tube, destroy the processus cochleariformis and avulse the tensor tympani.

It is not likely that this operation will leave much useful hearing.

Popper's route (1946*a*) (fig. 7).—Mention must also be made of Popper's route in which extra space is obtained by partial excision of the tympanic plate. The route is proposed really for fenestration and similar procedures for which indeed it may have real value. Popper has, however, suggested that his route might be useful in otorrhœa. This is unlikely for the following reasons: The surgeon will be reluctant to open up clean tissue spaces—especially close to the temporo-mandibular articulation in the presence of chronic sepsis. Furthermore there is no real need for the extra space thus obtained in view of the fact that ample exposure is already obtained by the technique herein described.

Indications.—The fundamental difference between atticotomy on the one hand and ossiculectomy and classical mastoidectomy on the other hand is most clearly brought out in considering the treatment of attic suppuration presenting via a small perforation in Shrapnell's membrane. The discharge is minimal but intractable. The hearing commonly remains excellent for many years. In these cases ossiculectomy is mischievous. It inevitably impairs hearing and may not cure the suppuration. Radical mastoidectomy has just as bad an effect on hearing and leaves a large cavity which may continue to discharge even more than before. Atticotomy achieves exactly what McKenzie proposed. I have performed the operation frequently in this sort of case and almost always preserved the incus. The tiny cavity heals remarkably quickly and the hearing remains excellent. It should, however, not be imagined that atticotomy is only indicated in this limited group of cases. On the contrary, I would say that once a surgeon has fully mastered the technique he will use it to the exclusion of all others. The only exceptions are: (1) Cases in which intracranial or other complications are definitely suspected. (2) Cases in which the soft tissues of the meatus have become chronically thickened and deny access to the deep meatus.

Acknowledgments.—I am happy to acknowledge my indebtedness to Mr. R. L. Plackett for the statistical analysis and to Mr. H. Zalin who has assisted me indefatigably, not only in the theatre, but also in the Out-Patient Department, where the vitally important after-treatment is given.

On the use of Zelex penicillin:

(1) The Zelex should be dry sterilized in small quantities in separate test tubes.
(2) Any moisture during sterilizing will denature it.
(3) Even at best there is always some impairment of the "gelling" quality. Therefore a batch should never be re-sterilized. Throw any surplus away.
(4) Mix the powder with penicillin solution of required strength. I use 5,000 units per c.c. The proportions required are easily determined by trial.
(5) When the mixture is still fluid suck it up into a Watson-Williams syringe using the straight sphenoidal cannula.
(6) Wait till the mixture has set to a gel, i.e. it just emerges from the cannula in a semi-solid consistency.
(7) Squirt it into the cavity under direct vision.
(8) Zelex must not be poured in whilst still fluid. It can seep under flaps or into the middle-ear cleft and act as a foreign body.
(9) Remove seven to fourteen days later by gentle syringing and if necessary morcellement.

BIBLIOGRAPHY

LEMPERT, J. (1938*a*) *Arch. Otolaryng., Chicago*, 27, 573.
—— (1938*b*) *Arch. Otolaryng., Chicago*, 27, 587.
—— (1938c) *Arch. Otolaryng., Chicago*, 27, 572.
MCKENZIE, D. (1931) *J. Laryng.*, 46, 163.
POPPER, O. (1946*a*) *J. Laryng.*, 61, 24.
—— (1946*b*) *J. Laryng.*, 61, 441.
SHAMBAUGH, G. E., Jr. (1937) Year Book of Eye, Ear, Nose and Throat. Chicago, 386.
THIES, C., and THIES, F. (1912) *Arch. Ohrenheilk.*, 89, 137.
TRAMPNAU (1935-36) *Z. Hals-Nas.-u. Ohrenheilk.*, 39, 203.

Mr. F. W. Watkyn-Thomas said that transmeatal methods had been practised for some eighty years, and although they had achieved success in the hands of gifted surgeons, they had never been generally accepted. The reason for this was that the difficulties of the operation made the methods unsuitable for general application. Mr. Tumarkin had mentioned and condemned removal of the outer attic wall by a punch with the transmeatal method. This was described by West and Scott in their "Operations of Aural Surgery", London, 1909. When he was their house surgeon five years later—in 1914—he was forbidden ever to try anything of the sort. He could not see that the results were in any way superior to the modified radical, or, say, the transmastoid atticotomy. Here in his experience, and, he thought, in that of many of his colleagues, there was no danger to the hearing. The hearing was usually improved. The access was much easier, and he could not agree that it was so necessary to remove the incus. If the incus was absolutely loose, lying in a mass of granulation, so that it came out of the end of a sucker, then he thought it was useless to leave it, but otherwise the incus could always be left intact. In fact one's guide for the operation should be to see the crus of the incus lying on the external canal.

Then came the question of accessibility. The majority of cases of attic disease were due to cholesteatoma, and he knew of no method by which one could tell, except by full exposure, how far that cholesteatoma extended. If there was cholesteatoma one could not remove it except by removing the matrix, and if the matrix extended far back into the antrum he failed to see how a surgeon, even of Mr. Tumarkin's ability, could reach it and eliminate it.

The second question of accessibility was in cases in which there was a mastoid structure where one had compact bone with a central chain of cells which had been destroyed by suppuration and had left a cavity—an empyema—in the mastoid. He knew of no way of detecting that except by exposing it. Therefore, although he was impressed by Mr. Tumarkin's skill and his excellent results, he must regard his procedure as retrograde so far as mastoid suppuration was concerned.

Mr. R. L. Flett desired to support Mr. Tumarkin as against Mr. Watkyn-Thomas. Mr. Tumarkin generally tried by previous X-rays to find the limitations of work on the mastoid. He himself was very well satisfied with the transmeatal operation. He was also doing fenestrations through that route. He wished to pay a tribute to Mr. Tumarkin's method.

Mr. Terence Cawthorne said that he thought that some form of meatal approach was becoming more popular in operations for chronic suppurative otitis media. He had been accustomed for some years to using the endaural approach, and he could see that there might be some advantages for what Mr. Tumarkin described, but that it required suitable practice and considerable skill. Those who had seen large numbers of school children suffering from chronic suppurative otitis media would welcome the possibilities presented by this operation.

Mr. I. Simson Hall had found a great many points of interest in Mr. Tumarkin's paper, but he could not help feeling that if discharge continued in one of these cases, as discharge will in a small

(3) The effect on function is also gratifying. The following audiograms appertaining to four children (shown at the Otological Section of the Royal Society of Medicine on February 7, 1947) demonstrate what can be achieved in suitable cases. In each case there had been bilateral chronic suppurative otitis media for many years. Conservative treatment cured one ear but failed in the other. Atticotomy was then performed on the infected ear. In each case there was a substantial improvement in hearing although in no case was the operated side as good as the opposite side.

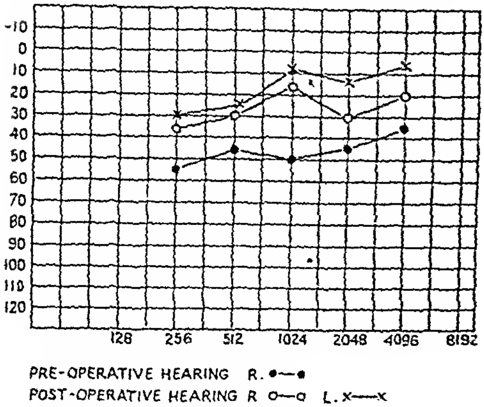


FIG. 8.—Audiogram of R. L., *aged 11*. History: Bilateral chronic suppurative *otitis media*, three years. Left ear recovered with conservative treatment. Right ear resisted treatment. Right ear—post-superior perforation with purulent otorrhœa. Operation: Right transmeatal atticotomy, 21.1.46. In hospital seven days. Ear healed in seven weeks. Incus preserved. Average hearing gain 21 db.

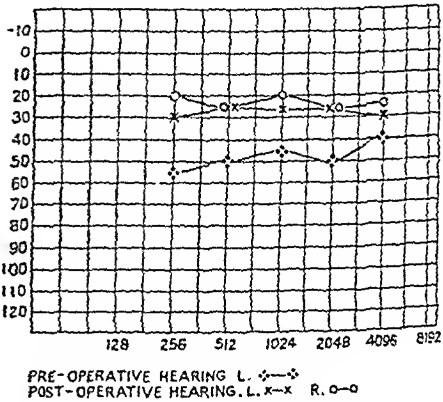


FIG. 9.—Audiogram of E. P., aged 13. History: Bilateral chronic suppurative otitis media, three years. Right ear recovered with conservative treatment. Left ear resisted treatment. Left ear—post-superior perforation with purulent otorrhœa. Operation: Left transmeatal atticotomy, 21.1.46. In hospital seven days. Ear healed in seven weeks. Incus preserved. Average hearing gain 21 db.

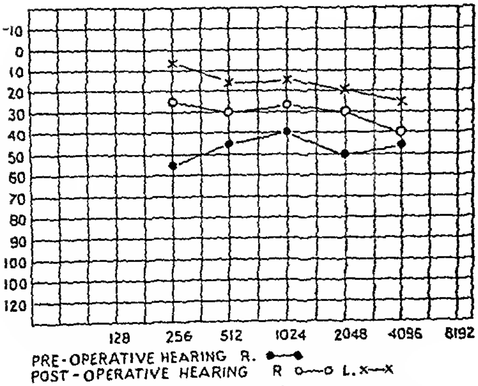


FIG. 10.—Audiogram of I. G., aged 10. History: Bilateral otorrhœa when teething, condition subsided but recurred when she entered school. Intermittent otorrhœa five years. Conservative treatment cured left ear, but failed to cure the right. Right post-superior perforation with purulent otorrhœa. Operation: Right transmeatal atticotomy. In hospital five days. Ear dry in seven weeks. Incus preserved. Average hearing gain 17 db.

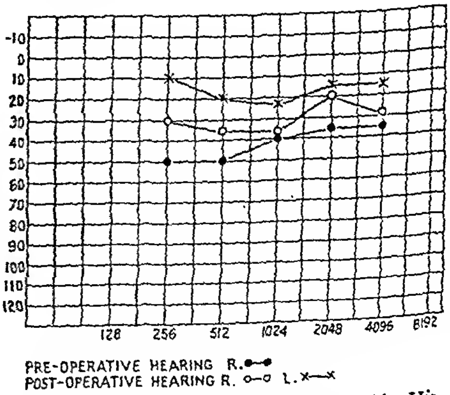


FIG. 11.—Audiogram of P. S., aged 11. History: Bilateral otorrhœa two years ago (also otorrhœa in infancy). Intensive conservative treatment for two months cured the left otorrhœa but not the right. Right ear—post-superior perforation with purulent otorrhœa. Operation: Right transmeatal atticotomy, 25.3.46. In hospital five days. Ear dry in six weeks. Incus preserved. Average hearing gain 12 db.

To sum up.—(1) Transmeatal attico-antrotomy is described and proposed as the method of choice for dealing with intractable non-complicated otorrhœa. (2) It is a minor operation from the patient's point of view. (3) It is possibly more difficult than transmastoid operations. (4) It is *not* a dangerous operation. (5) Its results are extremely satisfactory.

Acknowledgments.—I am happy to acknowledge my indebtedness to Mr. R. L. Plackett for the statistical analysis and to Mr. H. Zalin who has assisted me indefatigably, not only in the theatre, but also in the Out-Patient Department, where the vitally important after-treatment is given.

On the use of Zelex penicillin:

(1) The Zelex should be dry sterilized in small quantities in separate test tubes.
(2) Any moisture during sterilizing will denature it.
(3) Even at best there is always some impairment of the "gelling" quality. Therefore a batch should never be re-sterilized. Throw any surplus away.
(4) Mix the powder with penicillin solution of required strength. I use 5,000 units per c.c. The proportions required are easily determined by trial.
(5) When the mixture is still fluid suck it up into a Watson-Williams syringe using the straight sphenoidal cannula.
(6) Wait till the mixture has set to a gel, i.e. it just emerges from the cannula in a semi-solid consistency.
(7) Squirt it into the cavity under direct vision.
(8) Zelex must not be poured in whilst still fluid. It can seep under flaps or into the middle-ear cleft and act as a foreign body.
(9) Remove seven to fourteen days later by gentle syringing and if necessary morcellement.

BIBLIOGRAPHY

LEMPERT, J. (1938*a*) *Arch. Otolaryng., Chicago*, 27, 573.
—— (1938*b*) *Arch. Otolaryng., Chicago*, 27, 587.
—— (1938*c*) *Arch. Otolaryng., Chicago*, 27, 572.
McKENZIE, D. (1931) *J. Laryng.*, 46, 163.
POPPER, O. (1946*a*) *J. Laryng.*, 61, 24.
—— (1946*b*) *J. Laryng.*, 61, 441.
SHAMBAUGH, G. E., Jr. (1937) Year Book of Eye, Ear, Nose and Throat. Chicago, 386.
THIES, C., and THIES, F. (1912) *Arch. Ohrenheilk.*, 89, 137.
TRAMPNAU (1935-36) *Z. Hals-Nas.-u. Ohrenheilk.*, 39, 203.

Mr. F. W. Watkyn-Thomas said that transmeatal methods had been practised for some eighty years, and although they had achieved success in the hands of gifted surgeons, they had never been generally accepted. The reason for this was that the difficulties of the operation made the methods unsuitable for general application. Mr. Tumarkin had mentioned and condemned removal of the outer attic wall by a punch with the transmeatal method. This was described by West and Scott in their "Operations of Aural Surgery", London, 1909. When he was their house surgeon five years later—in 1914—he was forbidden ever to try anything of the sort. He could not see that the results were in any way superior to the modified radical, or, say, the transmastoid atticotomy. Here in his experience, and, he thought, in that of many of his colleagues, there was no danger to the hearing. The hearing was usually improved. The access was much easier, and he could not agree that it was so necessary to remove the incus. If the incus was absolutely loose, lying in a mass of granulation, so that it came out of the end of a sucker, then he thought it was useless to leave it, but otherwise the incus could always be left intact. In fact one's guide for the operation should be to see the crus of the incus lying on the external canal.

Then came the question of accessibility. The majority of cases of attic disease were due to cholesteatoma, and he knew of no method by which one could tell, except by full exposure, how far that cholesteatoma extended. If there was cholesteatoma one could not remove it except by removing the matrix, and if the matrix extended far back into the antrum he failed to see how a surgeon, even of Mr. Tumarkin's ability, could reach it and eliminate it.

The second question of accessibility was in cases in which there was a mastoid structure where one had compact bone with a central chain of cells which had been destroyed by suppuration and had left a cavity—an empyema—in the mastoid. He knew of no way of detecting that except by exposing it. Therefore, although he was impressed by Mr. Tumarkin's skill and his excellent results, he must regard his procedure as retrograde so far as mastoid suppuration was concerned.

Mr. R. L. Flett desired to support Mr. Tumarkin as against Mr. Watkyn-Thomas. Mr. Tumarkin generally tried by previous X-rays to find the limitations of work on the mastoid. He himself was very well satisfied with the transmeatal operation. He was also doing fenestrations through that route. He wished to pay a tribute to Mr. Tumarkin's method.

Mr. Terence Cawthorne said that he thought that some form of meatal approach was becoming more popular in operations for chronic suppurative otitis media. He had been accustomed for some years to using the endaural approach, and he could see that there might be some advantages for what Mr. Tumarkin described, but that it required suitable practice and considerable skill. Those who had seen large numbers of school children suffering from chronic suppurative otitis media would welcome the possibilities presented by this operation.

Mr. I. Simson Hall had found a great many points of interest in Mr. Tumarkin's paper, but he could not help feeling that if discharge continued in one of these cases, as discharge will in a small proportion of all operations, it would be very difficult for him to satisfy himself that some diseased cells had not been overlooked, but as Mr. Tumarkin had not quoted any figures he assumed that Mr. Tumarkin was satisfied that in his hands this operation gave better results than any other form of radical mastoidectomy in suitable cases.

Mr. W. Ogilvy Reid spoke of the unfortunate tendency to recurrence of mastoid infection in children. Children seemed to be liable to acute reinfection of the mastoid cavity subsequent to operation. Some time before the late Mr. G. J. Jenkins died he was working with him on a periosteal-flap operation which he (Mr. Reid) later published in 1942 (*J. Laryng.*, 57, 405), the aim being to try to prevent the spread of any subsequent infection of the middle ear to the mastoid cavity formed by the operation. That flap operation had been very effective in limiting the spread, confining it to the middle ear. He wished to ask Mr. Tumarkin whether he had found the recurrence rate diminished in any way by his particular technique. He wondered whether the provision of drainage from the attic cut short any subsequent attack of otitis media.

Mr. A. Tumarkin, in reply, said that Mr. Watkyn-Thomas had raised what were, after all, the standard objections to the operation, and short of repeating what he had already said in the paper he could not say any more in answer to his objections. He believed that no particular difficulty would stand in the way of any competent surgeon carrying out what he had advised.

Mr. Cawthorne had spoken of skill in the operation and in the after-treatment. One of the essential features of attico-antrotomy was that the after-treatment was simplicity itself. Members must have been struck by the rapidity of healing in many of the cases he had shown. Of course, cases did come along which involved special difficulty; nevertheless, when he did an attico-antrotomy he expected to syringe the Zelex out a week or ten days later and to see the patient thereafter once a week for a month and, at the end of that time, no more trouble.

Mr. Simson Hall had asked for statistics, but he did not know how his own figures could be quoted with any real significance against somebody else's. Attico-antrotomy was an operation based on a definite conception of pathology. It set out to do certain things and it did them. Actually he would say quite definitely that he could get better results than he ever got with any other operation. He expected the operation cavity to dry and he was disappointed if it did not.

When the ear continued to discharge it discharged from the middle ear. His case No. 1 was a man who had a radical operation in childhood. His other ear became infected, and he came to him after eighteen months obviously very deaf. He treated him for three months before he finally operated. He operated and preserved the incus. The middle ear was still moist, but instead of a gross purulent discharge, there was a slight mucoid discharge which came from the middle ear. Ears which did not dry after an attico-antrotomy failed to do so because of discharge seeping from the middle ear and not from the mastoid. In the cases of partial cure the partiality of the cure was not due to disease in the mastoid, and those cases which did persist were reduced in number if operated earlier. Early operation was a necessity. He was thinking not so much about adults, but about children. Many children of the working classes had bilateral otitis media, and were going to be crippled if surgeons did not save them. He had brought 4 of them to that meeting, and he had done 35 cases during the year; every one of those 35 had a dry cavity.

Complications did occur after radical operation, but they should not be common. He did not suggest that these occurrences were a grave disadvantage of the radical, but still they did occur.

On the question raised by Mr. Reid as to whether attico-antrotomy was effective when the child got an acute ear, it was essential to distinguish quite clearly between acute otitis media and the chronic infection for which he did this transmeatal attico-antrotomy. Most of these children did not have a properly developed pneumatic system of their mastoid, and they were not liable to typical acute mastoiditis. Cases were seen in which the ear continued to seep discharge from the eustachian orifice, but not from the attic if an attico-antrotomy had been done. The child was not liable to acute mastoiditis because the mastoid was not pneumatized.

As to how one managed a procedure which was sometimes said to demand three hands, there was no difficulty in putting in the speculum, but it must fit tightly.

The President, in closing the discussion, said that he was familiar with Mr. Tumarkin's work and the good results which, in chronic middle-ear suppuration, followed his operations by the external meatal route, but as Mr. Watkyn-Thomas had remarked, many of us, accustomed to operate from behind the auricle, found it easier to do so and further cholesteatomatous invasion at times was remarkably extensive, filling the cells of the mastoid apex even in young children.

The more slender standard gouges appeared too thick in the shaft for these operations though Mr. Tumarkin had had some improved in the workshop. He had also spoken of the use of "the third hand". He (the President) made use of this regularly in the intranasal approach to the bone overlying the lacrimal sac and in "taking down" the crest in operations on the nasal septum.

Perhaps an assistant in the role of "Blacksmith's striker" might also be helpful to those deciding to operate upon the tympanic attic and antrum by the meatal route. Regulation of the force applied had not been at all difficult in intranasal work.

Section of Medicine

President—MAURICE DAVIDSON, M.D.

[*April* 22, 1947]

DISCUSSION: THE MANAGEMENT OF PATIENTS WITH ESSENTIAL HYPERTENSION

Dr. Geoffrey Evans, in opening the discussion, referred to the differential diagnosis between symptomatic and essential hypertension. In discussing the ætiology of essential hypertension Dr. Evans referred in the first place to the constitutional factor, that is to say, inheritance, which may determine not only the development of hypertension in a person, but also its location (in terms, for instance, of cerebral vascular disease or hypertensive heart disease) and the age of onset of symptoms. Although the predisposition to hypertension may be inherited, family influence and environment may be the factors which determine its development. Continued over-fatigue and exhaustion undoubtedly aggravate hypertension and, perhaps, on occasion, cause it. The background, therefore, of the patient's life, as well as the outlook and emotional state, need to be taken into account in advising a patient with essential hypertension, and Dr. Evans emphasized the importance of a sanguine outlook in the management of such a case. In discussing the detail of treatment, living within the limits of the individual's strength and the prescription of extra rest was the general rule. The most intensive form of conservative treatment consists of a preliminary period of rest in bed with sedatives, such as phenobarbitone, bromide or chloral; a diet of limited calorie value should be prescribed for all those who are over-weight, and in some cases it seemed that a restricted fluid intake, restriction of salt, alcohol, tea, coffee or tobacco, might do good; but a little alcohol taken with meals acted as a sedative and probably did no harm, and the same comment probably applied to tea, coffee and tobacco in moderation. In those with peripheral congestion venesection might do good, and for those with circulatory failure small doses of digitalis were given as a routine. For obesity Dr. Evans advised the fruit, vegetable and meat diet of Dr. Gardiner-Hill or the high protein diet of the late Dr. Dennis Embleton. Dr. Evans spoke at some length on the value of potassium thiocyanate, especially in respect of relief of headache and giddiness in hypertensive subjects, and the fall of blood-pressure in some cases. Dr. Evans remarked that in spite of eleven years' experience of the intensive treatment of essential hypertension with potassium thiocyanate therapy in the hands of physicians, and an equally long history of lumbar and dorsilumbar sympathectomy in the hands of surgeons, the value of these forms of treatment is not yet fully agreed. The reason for this he believed to be due to the association of hypertension with arteriosclerotic disease, and especially due to the fact that in some patients the arteriosclerotic process of disease might be continually active and progressive, whereas in others there were phases of activity with long periods of quiescence. The disease, in fact, consists of functional and structural components. The functional components are a generalized hypertonia of the systemic circulation which is responsible for the hypertension, and localized vascular spasm which is especially responsible for many of the clinical manifestations of the disease, including retinal exudates and hæmorrhages, cerebral vascular accidents, hypertensive heart disease (he thought), and renal complications in some cases. It seemed to him that disorders of vascular tone might cause such symptoms as headache and giddiness from time to time, or for a number of years, without necessarily causing a coincident change in vascular structure. Such a case might be stationary in spite of symptoms. On the other hand patients with hypertension and a more stable vasomotor control would be symptom-free. But in another group of cases, coincident with alteration in vessel tone, structural changes in the blood-vessels took place, and a condition of active arteriosclerotic disease was present. This state of activity could be recognized by the presence of hæmorrhages in various parts of the body, including retinal hæmorrhages and microscopic hæmaturia, epistaxis, menorrhagia, hæmoptysis, hæmatemesis and melæna. In other cases thrombotic phenomena registered the activity of arteriosclerotic disease. Evidence of active disease was also to be looked for in alterations in the electrocardiogram, in the urine, in the peripheral circulation in the lower extremities, and it was generally present in patients whose diastolic pressure was over 120 mm.Hg. In fact the difficulty of assessing the value of either intensive medical or surgical treatment was due to the impossibility at present of forecasting the natural course of arteriosclerotic disease in a hypertensive subject. No method of treatment at present available could be relied on to prevent the recurrence of active phases of arteriosclerotic disease in some subjects or prevent the continued progress of the disease in others.

Mr. A. Dickson Wright said that the surgical management of the case of hypertension was by no means standardized, and it was very difficult to be dogmatic in a disease so variable in its course and effects. The ineffectiveness of medical treatment and the lethal character of the disease brought surgery into the picture possibly only as a stop-gap until an effective medical treatment or prophylaxis based on sound physiology was evolved, but, nevertheless, in selected cases a valuable way out of an awkward position lay with surgery for the unfortunate patient afflicted with this distressing complaint.

Selection was the most important step in the surgical handling of these cases. If hopelessly advanced cases were submitted to operation the method would be discredited, the surgeon's time wasted and the patient and relatives bitterly disappointed. In the selection of cases many factors had to be considered and sometimes surprisingly good results were obtained in patients with rather poor prospects. It was unusual to operate on patients over 50 years old although some patients over 60, generally in the upper social classes, were being treated surgically in the United States of America. Females did better than males surgically just as they did medically, and especially hopeful were those cases in which the high blood-pressure of pregnancy toxæmia became established permanently. The patient with a ruddy complexion did better than his pallid counterpart with the same blood-pressure. Patients with hopelessly damaged kidneys were avoided although nephritis was not an absolute contra-indication, it being felt that the reduction of the filtration pressure would help the damaged renal tissue and reduce the albumin loss. A renal function of at least 65% of normal was essential for cases for surgery, but there were great fallacies in these renal tests, and they should be repeated and checked to eliminate error.

A severely damaged heart was another definite contra-indication and pulsus alternans, cardiac asthma and Cheyne-Stokes' breathing should put operation out of question. Angina and lesser degrees of myocardial damage were not contra-indications, and the inverted T wave had returned to normal in some cases as recorded by White of Boston. In certain cases of angina a left cervical sympathectomy added to the pressure-reducing operation might turn a partial cure into a complete one as far as the angina was concerned.

Severe cerebral damage from thrombosis or hæmorrhage was a complete contra-indication but cases with minor residual damage had been done with fair results.

Blindness or near blindness were also contra-indications, and many regarded established papillœdema and the "tiger skin" fundus as indications of the unsuitable case. Early retinal damage was an indication of urgency, and there was little doubt that the surgical reduction of blood-pressure often saved the eyes from irretrievable damage.

Severe encephalopathy was unfavourable as regards prognosis but provided the surgeon with his greatest incentive to operate. To rid the patient of blinding headaches, vertigo and mental obfuscation and, most important of all, transient hemiplegias and hemianæsthesiæ was indeed a cause for gratification. One felt little patience for those who criticize successes in this respect saying that encephalopathy manifestations are functional even though they afflicted the most stolid types and children before they had ever learnt to be "functional".

A high pulse-pressure was very unfavourable, gross thickening of the arteries also and a high sleeping blood-pressure. A lumbar puncture pressure of over 300 was regarded by others as an unfavourable prognostic sign.

The sedation tests were very valuable for estimating the lability of the blood-pressure, this could be quickly done with pentothal intravenously provided a full dose was used and the deepest anæsthesia produced. Another way was the sodium amytal test, 3 grains being given hourly till the patient was unrousable and pressures taken at regular intervals while the drug was effective. A substantial fall obtained by either method was a direct encouragement to operate.

Intravenous pyelography disclosed cases of renal disease which could be remedied by surgery, such as atrophic pyelonephritis, calculus, tuberculosis, pyonephrosis, &c., but as operations for unilateral disease only produced a cure in 30% of cases it was wise, when dealing with the kidney condition, to supplement it with a sympathectomy so that if the case was a failure from the unilateral kidney point of view only one more operation was necessary to give him the *full* benefit of sympathetic surgery.

Coarctation of the aorta was eliminated by observing the femoral pulses and if found the coarctation should be excised.

Adrenal neoplasms caused hyperpietic crises due to adrenaline release and were dealt with appropriately. More difficult was high tension due to basophilic adenoma of the pituitary. Uterine myomata, prostatic or urethral obstruction and lead poisoning were all dealt with before regarding a case as one of essential hypertension. Addiction to benzedrine or ephedrine must be thought of in these high-pressure days.

The first suggestion that high blood-pressure could be reduced by cutting the sympathetic nerves came from Kraus of Berlin. The first series operated upon were done at the Mayo Clinic by Adson and his confrères who cut the anterior nerve roots of the lower six dorsal nerves through an extensive laminectomy. This was a great mutilation and did not last although some good results were obtained. Adson then simplified his operation to a renal incision of each side at a ten-day interval and removed all three splanchnic nerves and the first two lumbar ganglia with removal of half the adrenal (optional) and biopsy of the kidney. He claimed remarkably good results from this operation, and it was noticed that many of the patients with a maintained blood-pressure after operation had nevertheless a great mitigation of symptoms. This operation of Adson's is very simple, disturbs the patient very little, has practically no complications or death-rate and is followed by only minor discomfort.

Peet has done a single-stage operation on a very large series and operates through the posterior mediastinum, removing the eleventh and twelfth ribs on both sides and extracting as many of the lower dorsal ganglia as possible and the splanchnics before they pierce the diaphragm.

Smithwick combined the two operations and extended the operation in an upward direction by means of special illuminated retractors claiming a much more radical removal including certain small contributions to the aortic plexus missed by both the other operations. Both Peet's and Smithwick's operations can be followed by troublesome intercostal neuralgia, abdominal wall palsies, pleural and mediastinal exudates and this price as well as a higher mortality rate must be paid for the more extensive sympathectomies.

Poppen has endeavoured to make the Smithwick operation easier in its upper extension by making another window into the posterior mediastinum by removing the seventh or eighth rib through a separate incision.

Grimson has opened the chest widely through two rib spaces, fourth and eighth, and removed the whole dorsal ganglionic chain by the transpleural route. Then if this did not suffice the abdominal sympathetic chains were removed at a third operation and if the blood-pressure still remained undiminished it could be safely described as humoral. This large operation carried a considerable death-rate (15%) and had not been widely adopted although it was *the* only radical sympathectomy, the others having varying degrees of partiality. Equally good figures of benefit have been reported for all the operations but all figures have to be received with great caution. It is possible to get varying blood-pressure (and even E.C.G.) in the same patient according to the depth of respiration, posture, mental state and so on. The price paid for the more extensive sympathectomies in the way of pain, complications and death-rate might be rather too much to pay in contrast with the small degree of discomfort and quite good results obtained by a thorough Adson sympathectomy done under spinal anæsthesia.

An attempt had been made recently to treat the very severe cases of malignant hypertension with papillœdema by resecting so much adrenal that a near-Addison's disease was produced (some patients even becoming pigmented). There seemed to be some hope for the hopeless by this procedure especially when combined with a sympathectomy, but the reactions after subtotal adrenalectomy were very severe, and there was a considerable death-rate. In a few very severe cases artificial arteriovenous fistula had been made in the neck. These staved off the evil day of blindness or cerebral hæmorrhage and could be closed quite easily when the heart grew tired of feeding the fistula. A remarkable fall in blood urea occurred in these cases, the reason for it might repay investigation.

Dr. C. H. Wyndham: *Sympathectomy in hypertension.*—Dr. Wyndham said that in spite of the present enthusiasm for the surgical treatment of hypertension, we were in the inevitable time-lag during which evidence, in a sufficiently large series of cases over a sufficient number of years, was accumulated and would or would not indicate the clinical justification of the procedure. It was of interest to re-examine, therefore, the original aims of the authors of the procedure in the light of evidence that had accumulated on the effects of sympathetic deprivation.

Adson and Brown were early in the field—first case of sympathectomy for hypertension was done in 1925—and they began a series in 1930. They based their expectancy of a fall of blood-pressure to follow on a "maintained vasodilatation of arteries in the sympathectomized area". That this result would follow sympathectomy was concluded from a series of acute observations on the skin temperature increase, extending over not more than nineteen days, in local sympathectomy. The observation of a fall in blood-pressure after spinal anæsthesia was attributed to the same mechanism and the fall of blood-pressure was used as an argument in favour of an anticipated drop of blood-pressure on surgical sympathectomy.

Their emphasis on the fact that the new blood-pressure adjustment was due to "maintained vasodilatation of the arteries in sympathectomized area" and solely to the drop of the total peripheral resistance offered to the outflow of blood from the arterial circuit has been accepted and has obscured thought on the mechanism of sympathectomy in hypertension.

Recent work on circulatory dynamics has thrown into relief the constant interplay of both the central and the peripheral factors at work in cardiodynamic adjustments.

Dr. Wyndham continued: The blood-pressure in the arterial circuit is dependent largely on both the amount of blood pumped into the circuit and the resistance offered by the *total tone of the arterioles* to the outflow of blood from the circuit:

$$\text{B.P.} = \text{C.O.} \times \text{T.P.R.}$$

The litre volume per minute pumped into the circuit was shown to be related to two main factors: (*a*) The venous filling pressure; (*b*) the rate of the heart; and probably hormonal factors which have a direct effect on cardiac muscle action. An increase of either (*a*) or (*b*) causes an increase of cardiac output in a direct linear relationship.

At the other end of the circuit the resistance offered to the outflow of blood depends on the tone of arterioles of the three major vascular beds—skin, muscle and splanchnic areas. The flow through these areas is influenced, and in no constant manner, from one to the other by: (*a*) Metabolic state; (*b*) temperature; (*c*) hormonal content of perfusing blood; (*d*) sympathetic nervous control.

The manner in which these factors operate had been demonstrated when normal volunteers were bled up to 1,500 c.c. of blood, the following results being observed:

(i) Right auricular pressure, reflecting the venous filling pressure, falls. Since there is a steady fall of the right auric. pressure during bleeding it suggests that there is no immediate increase of venous tone (McMichael and Sharpey-Schafer, 1944).

(ii) The fall of right auric. pressure usually leads to a fall in the cardiac output, in spite of some acceleration of the heart rate.

(iii) The arterial pressure is maintained up to a point in each subject when it falls suddenly and the heart slows, the vasovagal faint.

(iv) This sudden fall in the arterial pressure is not due to a further drop of the cardiac output but is due to a sudden vasodilatation in muscle arterioles (Barcroft *et al.*, 1944).

Effect of Sympathectomy on Circulatory Dynamics

It had been demonstrated that a local and immediate decrease in arteriolar tone occurs in the sympathectomized area (Grant and Holling, 1938). In view of the fact that the uninvolved area is capable of full vasoconstrictor activity, the effect on total arteriole tone is not known in the type of sympathectomy performed for hypertension.

It had been suggested that sympathetic denervation decreases venomotor tone (Smith *et al.*, 1939). A decrease in venomotor tone would, probably, lower the venous filling pressure of the right auricle. A fall in right auricular pressure led usually to a decrease in cardiac output. The length of time and the degree to which venomotor paralysis persisted after sympathectomy was conjectural. Clinical observation suggested that it was not enduring. It was important to establish, therefore, the part played by each of the factors, the loss of venomotor tone, and the loss of arteriolar tone in the mechanism of the arterial blood-pressure fall of sympathectomy.

If (*a*) % change of the "mean" blood-pressure and (*b*) % change of the cardiac output can be calculated then the direction of change of the third factor, the "total peripheral resistance", can be assessed and compared with normal subjects.

It was now a practical procedure by the method of right auricular catheterization, to measure the alteration of the filling pressure of the right auricle and the change in cardiac output caused by sympathetic denervation in hypertensives.

Finally, evidence was accumulating on the relative efficacy of sympathectomy in producing vasodilatation and in its capacity to maintain this effect on arterioles. The following observations were made by Barcroft *et al.* (1943, 1944):—

Blood Flow through Muscle in c.c./100 c.c. tissue/min.

At 35° C.	After local heat 45° C. 1943	After acute sympathectomy 1944
4·0 c.c.	18 c.c.	7–8 c.c.

This suggests that in one of the major vascular beds, sympathectomy is not as effective a vasodilator as local heat. Local exercise apparently has an even greater vasodilator effect. That this twofold increase is not maintained even at this level was shown by Grant and Holling (1938).

We were now in a position to comment on Adson and Brown's original claim and to suggest that:

(*a*) Sympathectomy might act in reducing arterial pressure, both by the effect on arteriole tone, thereby decreasing total peripheral resistance, and possibly by an effect on venomotor tone, thereby decreasing cardiac output.

(*b*) That it produces less effect on the total capacity of arterioles in muscle to vasodilate than local heat or local exercise. It is highly improbable that this initial decrease in tone is maintained.

BIBLIOGRAPHY

ADSON and BROWN (1934) *J. Amer. med. Ass.*, **11**, 1115.
BARCROFT, H., and EDHOLM, O. G. (1943) *J. Physiol.*, **102**, No. 1, 5.
——, —— (1945) *J. Physiol.*, **104**, 161.
——, ——, MCMICHAEL, J., and SHARPEY-SCHAFER, E. P. (1944) *Lancet* (*i*), 489.
GRANT, T., and HOLLING, H. (1938) *Clin. Sci.*, **3**, No. 3, 273.
MCMICHAEL, J., SHARPEY-SCHAFER, E. P. (1944) *Brit. Heart J.*, **6**, 33.
SHARPEY-SCHAFER, E. P. (1944) *Clin. Sci.*, **5**, 125.
—— (1945) *Lancet* (ii), 296.
SMITH, H. W., ROVENSTINE, E. A., GOLDRING, W., CHASIS, H., and RANGES, H. A. (1939) *J. clin. Invest.*, **18**, 319.
WALLACE, J., and SHARPEY-SCHAFER, E. P. (1941) *Lancet* (ii), 393.

Mr. H. J. B. Atkins pointed out that in Mr. Dickson Wright's large series there was a remarkably low mortality, but that in one case cerebral thrombosis had developed. In his very much smaller series he had had a case of retinal thrombosis on the third day after operation with the development of a permanent blindness in that eye. As the consequences of thrombosis in the heart, the brain and the eye were so much more serious than thrombosis elsewhere, and as it was in these sites that thrombosis was likely to follow the operation for hypertension, Mr. Atkins inquired whether the incidence was sufficiently high in Mr. Dickson Wright's experience to merit the injection of heparin as a routine after this operation.

Dr. Evan Bedford said that by far the commonest cause of death in essential hypertension was heart failure, which occurred in 60 to 70% of all cases, compared with about 20% dying of cerebral vascular accidents and less than 10% of renal failure. Therefore, the management of patients with hypertension should be directed especially to the care of the heart.

The natural course of the disease was one of gradually progressive cardiac enlargement extending over a period of ten to thirty years and terminating in heart failure, either congestive or anginal. Coronary disease was frequently associated with hypertension, and angina pectoris or coronary occlusion occurred in 30 to 40% of cases. The rate at which the heart enlarged was almost imperceptible from year to year, in the absence of failure, and by measuring serial orthodiagrams over periods up to fourteen years he had found the average increase in transverse diameter to be less than 2 mm. per year. Once the stage of left heart failure was reached, rapid cardiac enlargement often occurred.

He quoted Dr. Paul White as stating that the crux of the treatment of hypertensive heart disease was not the imposition of an invalid life or the support of the heart with digitalis, &c., but the control of the hypertension itself. However, as yet we had no medical means of accomplishing this. Evans and Loughnan (1939) had made a systematic and painstaking investigation of 33 drugs, including thiocyanates, which had been advocated in treating hypertension, testing each remedy against a placebo as control, over a reasonable period of time, and they had shown conclusively that none of these drugs was hypotensive.

Thiocyanate had been in use for over twenty years without convincing the majority of physicians that it could effectively control hypertension. Admitting that thiocyanate was sometimes successful in relieving symptoms, as in cases which Dr. Geoffrey Evans had cited, it was usually too toxic or too disappointing to offer any serious solution to the problem of preventing hypertensive heart disease.

If we had no means of removing the burden on the heart, we could at least minimize it by prescribing suitable restrictions, and prevent the superimposition of additional burdens in the form of obesity, alcoholism, overeating, excessive smoking, and the stresses of a high-pressure life. Patients with hypertension must learn to live slowly and, in accordance with modern ideas, the heart required *a forty-hour week*. He was confident that regular medical supervision and the imposition of a suitable régime could slow the progress of the heart disease and thus prolong life. Each patient needed his mode of life carefully planned, and a timetable should be worked out which allowed adequate time for sleep and rest in bed, and which excluded all unessential physical and psychological stresses.

When the hypertensive heart failed, the ordinary treatment for heart failure was indicated, namely an adequate period of complete rest in bed, restriction of fluids and salt, digitalization, and mercurial diuretics. Albuminuria and a slightly raised blood-urea were not contra-indications to mercurial diuretics in hypertensive heart failure. In the majority of cases, a stage of isolated left heart failure preceded signs of systemic venous congestion, and it was important to recognize and treat heart failure at this stage.

A triad of important signs of cardiac weakness gave warning of impending failure, namely gallop rhythm, pulsus alternans, and inversion of the T wave in lead I of the electrocardiogram, and in such cases attention should be focused on the lung bases and not the legs for the first appearance of œdema. Aminophylline was often of value in treating Cheyne-Stokes' respiration which was a common complication of hypertensive heart failure.

Finally, the indications for surgical treatment of hypertension had to be considered. Sympathectomy for hypertension had been introduced by Adson and Rowntree twenty years ago, and had been practised ever since, without becoming accepted as a reasonably effective method of treatment for general use. Great claims had recently been made for the more radical surgical procedure introduced by Smithwick of Boston, but, even in America, opinion as to its value and indications was by no means unanimous. It was already clear that this operation did not cure hypertension. It produced a significant reduction in blood-pressure in a proportion of selected cases, possibly about half. The question of when to employ surgical treatment was most important. It would seem rational to do so in the early stages of the disease, before the heart became involved, and no less a surgical authority than De Takats expressed the view that the only clear-cut indication for surgery in hypertension was a pressure constantly exceeding 140/90 mm. in subjects aged 18 to 25 years. He regarded surgery as debatable in the middle-aged hypertensive and as contra-indicated in malignant hypertension. Because the outlook seemed hopeless was not a proper reason for submitting a patient to surgical treatment unless it offered a reasonable chance of proving effective. Dr. Paul White believed that the cardiac changes in hypertension were in some measure reversible, and advocated surgical treatment for hypertensive heart disease.

Two quite distinct problems required solution, first the value of surgery in the early stages of the disease with a view to preventing heart disease, and secondly its value in the later or cardiac stages of the disease. The time has not yet arrived when surgical treatment could be regarded as generally applicable to patients with hypertension. The method required careful testing under controlled conditions, both in the early and the later stages of hypertension, before its indications could be decided, and the results needed to be carefully assessed by those with special experience of the disease.

REFERENCE

Evans, W., and Loughnan, O. (1939) *Brit. Heart J.*, 1, 199.

Dr. T. H. Whittington, speaking as an ophthalmologist, said that many cases of hypertension were first seen, and the diagnosis made, because of visual symptoms. The retina might be considered the extracranial part of the cerebral hemispheres, and the optic nerve homologous with the association tracts, and the retinal artery as a terminal branch of the intracranial circulation. Therefore, the ability to see these structures during life under a magnification of 15 to 20 times should be of importance in assessing the case. He suggested that careful observation of the signs in the fundus oculi, which had not been mentioned by speakers, should be made in all cases, and be added to the other clinical controls, in assessing the effects of medical and surgical treatment. The tragic loss of sight in one eye, due to a vascular catastrophe in it, and the danger of a similar occurrence in the other eye, might be considered, in the younger patients, as an indication for sympathectomy, but the results of treatment on the circulation in the eye could only be assessed if careful observation of the fundi was made in all cases having operation. For the same reason physician and ophthalmologist should collaborate in judging effects on retinal circulation when thiocyanate or other treatment was used.

Mr. A. Dickson Wright, in reply to Mr. Atkins, said that heparin had not been used to counteract these post-operative thromboses because the incidence was not sufficiently high; on the slightest sign of their appearance heparin treatment to the full extent would be indicated.

[*May* 27, 1947]

DISCUSSION: THE PRESENT POSITION IN REGARD TO THE PNEUMOCONIOSES

Dr. E. R. A. Merewether (*H.M. Senior Medical Inspector of Factories*): That over 500 deaths a year from pneumoconiosis should still occur in this country is something of a challenge—a challenge not only to us doctors but to all who have a specific contribution to make to the prevention and control of this, so venerable a disease.

Naturally enough, each of us will first look at so complex a problem from the angle of his own particular activities, and for me this resolves itself into the salutary and somewhat chastening task of trying to assess what knowledge is lacking for the solution of the social problems which have been associated with this disease throughout the ages, that is problems of prevention, control, disablement and rehabilitation.

Section (1), Subsection (2) of the Workmen's Compensation Act, 1943, states "In this Act, the expression 'pneumoconiosis' means fibrosis of the lungs due to silica dust, asbestos dust or other dust, and includes the condition of the lungs known as dust reticulation," and Section 57, Subsection (3) of the National Insurance (Industrial Injuries) Act, 1946, defines "pneumoconiosis" in the same words.

From the legal point of view, therefore, *for purposes of compensation*, the essential feature of pneumoconiosis is the presence of fibrosis of the lungs.

Many medical men and laymen generally take a more comprehensive, if less precise, view, and if asked what they understood by this expression will say, "Any affection of the lungs produced by dust."

Clearly, therefore, we must make plain our meaning when we use this word, and particularly so in a medical certificate or a radiological report, or difficulties and disappointments will arise if we raise possibilities of compensation where none exist.

I propose therefore to use the legal meaning of the term, and this leads us directly to the question of diagnostic criteria. We depend, of course, on the triad of occupational history, clinical examination, and X-ray appearances; of these, the results of the clinical and radiographic examination may be of doubtful significance, particularly the radiographic, but the occupational history, if accurately taken and thoroughly investigated, is always significant and may carry conclusive weight in conjunction with the other examinations.

The interpretation of the radiographic appearances is becoming exceedingly difficult.

Here definitely, I feel, is an aspect which urgently requires reassessment in the light of recent knowledge with the view of relating much more accurately cause and effect, of standardizing techniques and laying down scientific criteria for interpretation. How this can be achieved I am not competent to say, but evidently such research includes not only consideration of pure radiological technique, but the determination of the limits of normality in the X-ray picture of industrial lungs and differentiation between abnormal markings representing presence of dust with no disease and those representing dust with disease present or in the offing.

The X-ray appearances resulting from the reaction of the lungs to the stimuli of dusts in mixtures in different degrees of concentration and particle size, some of the constituents being inert, some fibrosis producers, some inhibitors of fibrosis, and some believed to be accelerators, but all diffractors of X-rays in varying degrees present a pretty problem for research and analysis.

In addition, further research into the correlation of morbid histology with the X-ray appearances, if done on a considerable scale, might produce invaluable data.

This both by close follow-up of human cases and by animal experiment. Hitherto radiography in this field has been as an indispensable aid to diagnosis; now we would like it also to serve as an aid to the assessment of disablement and as a real guide to prognosis. Both these aspects are of increased importance in connexion with the improved basis of compensation provided by the Industrial Injuries Act and in respect of new rehabilitation measures provided for by the Disabled Persons (Employment) Act of 1944, and the new factories provided by the Board of Trade for the suitable employment of pneumoconiotics.

The assessment of disablement in pneumoconiotics is a most difficult matter to set on a scientific basis since at present so much depends, at least in the earlier stages, on the reactions of the individual, both involuntary and voluntary, to exercise.

There are many other aspects on which the lack of fundamental data is hampering progress of which I shall mention only a few.

We do need a great deal more knowledge of incidence rates and morbidity rates for pneumoconiosis in the relevant occupations. Incidence rates should provide, over a period of time, a sensitive index of the efficiency of preventive measures. The risk of silicosis, for example, varies very much in different occupations, as also does the average severity of the cases.

An average of 6·6 deaths a year during the six years 1940–45 from silicosis in sandblasters is no measure of the risk unless we know the population of sandblasters. Actually it is small, and therefore a few deaths represent a high mortality rate. A number of years ago I estimated that 5·4% of a population of sandblasters died from silicosis or silicosis with tuberculosis in the space of three and a half years.

A very rough calculation, but sufficient to give an indication of the importance of this point, shows that while the number of deaths from silicosis in coalminers each year is over 38 times that of sandblasters, the mortality rate from silicosis per 1,000 sandblasters is some 18 times that of coalminers and probably higher.

We can get an idea of the comparative risk and severity in certain occupations by comparison of the average duration of employment in fatal cases of silicosis: these range from 8·4 years to 39·1 years, the overall average duration of employment of 902 fatal cases of silicosis being 34·1 years, that of 54 sandblasters being 12 years, and that of 154 fatal cases of asbestosis being 14·9 years.

Apart from susceptibility to tuberculosis, personal idiosyncrasy appears to loom large, but here again much more information is required.

More data on the effects of massive exposures of man to so-called inert dusts like pure french chalk are necessary. That much-loved and much-missed Leroy Gardiner, who so greatly advanced our knowledge in this field, used to refer to exposure to "insulting" concentrations of dust—a very apposite expression.

Another point of importance is that not everybody who contracts pneumoconiosis to a diagnosable degree dies of the disease: here again we need to know much more of such cases, for they have a great bearing on preventive measures. Moreover, a person can contract more than one type of pneumoconiosis. I have a specimen of a lung from a man who contracted silicosis which was diagnosable but unlikely to kill him; he subsequently contracted asbestosis which was the cause of his death, and the lung shows both conditions.

I have touched only on a few aspects which serve to illustrate the need for more and yet more knowledge in this great field of work if the relevant preventive and social legislation is going to be completely successful in attaining its aims. They are practical problems of applied research and the solutions to them are, I suggest, matters of urgency.

I have not discussed the possible role of inhibitors such as alumina in helping the prevention and treatment of pneumoconioses, nor such questions as the effects of silica in the form of fume, the so-called nascent action of freshly fractured quartz and flint, the differences between the effect of diatomaceous earth and flint, and the great field of research still unexplored in dust counting and analysis.

Dr. C. M. Fletcher commented on the complete absence of any instruction on the subject of pneumoconiosis in the medical student's training. He referred to figures and certification from coalminers' pneumoconiosis to show that the disease is of great importance and is crippling the industry in South Wales at present. He then referred to some findings of Dr. Alice Stewart in a survey of men certified from pneumoconiosis in South Wales, showing that after certification, the disease is commonly progressive, despite cessation of dust exposure. The finding of a raised sedimentation rate in most progressive cases suggests that this progression may be due to infection, possibly tuberculous, but the results of cultures of sputum have not so far lent support to this hypothesis.

Dr. Fletcher then referred to the many problems at present outstanding in this field to which the Pneumoconiosis Research Unit were directing their attention.

Professor Matthew J. Stewart (*Leeds*): I shall confine my remarks to two aspects of this subject, namely (1) what I propose to term subclinical silicosis and (2) certain pathological considerations in relation to asbestosis.

SUBCLINICAL SILICOSIS

That the healthy lung is capable of dealing effectively with even large quantities of silicious dust is a fact which is still insufficiently recognized. Everyone is familiar with the coal-black discoloration and enlargement of the hilar and tracheobronchial lymph glands of the middle-aged and elderly town-dweller and the blue-black mottling, often confluent, of the pleural surface of the lungs which result from the long-continued inhalation of coal dust and soot, but the fact that such dust invariably contains traces or even considerable quantities of silica is less generally appreciated. So long as the parenchyma of the lung is otherwise healthy, its power of clearance, by lymphatic drainage, of silicious dust is very great. This is clearly shown by the not infrequent discovery of silicotic lesions in the hilar and tracheobronchial lymph glands, and in the immediately subpleural pulmonary tissue, while the rest of the pulmonary parenchyma is completely free from any suggestion of silicosis. Occasionally even the upper abdominal lymph glands may be grossly silicotic without any recognizable lesion being present in the substance of the lungs. The affected lymph glands are usually greyish-black on section, instead of jet black as in the more purely anthracotic lesion. They are also harder in consistency and drier on section. For many years in the post-mortem room I have made use of a simple test for determining the extent to which an enlarged and blackened lymphatic gland is silicotic. If the freshly cut surface of such a gland is dried by dabbing it momentarily on a dry cloth (e.g. one's P.M. room coat), it will remain dry afterwards if the lesion is in any appreciable degree silicotic. In a purely (or almost purely) anthracotic lymph gland, on the other hand, the cut surface will again become moist and glistening as soon as it is removed from contact with the dry cloth. I have confirmed the value of this test on many occasions by subsequent histological examination.

Now these lymph-gland and subpleural lesions are, in general, mere casual findings at autopsy in persons dying from other and quite unrelated diseases. Women are

This both by close follow-up of human cases and by animal experiment. Hitherto radiography in this field has been as an indispensable aid to diagnosis; now we would like it also to serve as an aid to the assessment of disablement and as a real guide to prognosis. Both these aspects are of increased importance in connexion with the improved basis of compensation provided by the Industrial Injuries Act and in respect of new rehabilitation measures provided for by the Disabled Persons (Employment) Act of 1944, and the new factories provided by the Board of Trade for the suitable employment of pneumoconiotics.

The assessment of disablement in pneumoconiotics is a most difficult matter to set on a scientific basis since at present so much depends, at least in the earlier stages, on the reactions of the individual, both involuntary and voluntary, to exercise.

There are many other aspects on which the lack of fundamental data is hampering progress of which I shall mention only a few.

We do need a great deal more knowledge of incidence rates and morbidity rates for pneumoconiosis in the relevant occupations. Incidence rates should provide, over a period of time, a sensitive index of the efficiency of preventive measures. The risk of silicosis, for example, varies very much in different occupations, as also does the average severity of the cases.

An average of 6·6 deaths a year during the six years 1940–45 from silicosis in sandblasters is no measure of the risk unless we know the population of sandblasters. Actually it is small, and therefore a few deaths represent a high mortality rate. A number of years ago I estimated that 5·4% of a population of sandblasters died from silicosis or silicosis with tuberculosis in the space of three and a half years.

A very rough calculation, but sufficient to give an indication of the importance of this point, shows that while the number of deaths from silicosis in coalminers each year is over 38 times that of sandblasters, the mortality rate from silicosis per 1,000 sandblasters is some 18 times that of coalminers and probably higher.

We can get an idea of the comparative risk and severity in certain occupations by comparison of the average duration of employment in fatal cases of silicosis: these range from 8·4 years to 39·1 years, the overall average duration of employment of 902 fatal cases of silicosis being 34·1 years, that of 54 sandblasters being 12 years, and that of 154 fatal cases of asbestosis being 14·9 years.

Apart from susceptibility to tuberculosis, personal idiosyncrasy appears to loom large, but here again much more information is required.

More data on the effects of massive exposures of man to so-called inert dusts like pure french chalk are necessary. That much-loved and much-missed Leroy Gardiner, who so greatly advanced our knowledge in this field, used to refer to exposure to "insulting" concentrations of dust—a very apposite expression.

Another point of importance is that not everybody who contracts pneumoconiosis to a diagnosable degree dies of the disease: here again we need to know much more of such cases, for they have a great bearing on preventive measures. Moreover, a person can contract more than one type of pneumoconiosis. I have a specimen of a lung from a man who contracted silicosis which was diagnosable but unlikely to kill him; he subsequently contracted asbestosis which was the cause of his death, and the lung shows both conditions.

I have touched only on a few aspects which serve to illustrate the need for more and yet more knowledge in this great field of work if the relevant preventive and social legislation is going to be completely successful in attaining its aims. They are practical problems of applied research and the solutions to them are, I suggest, matters of urgency.

silicosis in both mediastinum and upper abdomen, but the lungs were hardly affected. The cause of death was congestive heart failure with great cardiac hypertrophy, apparently due to intense indurative mediastinitis with complete obliteration of the pericardium and both pleural sacs. To this the glandular silicosis may well have contributed, but there was evidence also of old rheumatic valvular disease, although without serious mechanical defect.

PULMONARY ASBESTOSIS

The contrast between silicosis and asbestosis in respect of the character and distribution of the lesions is now well established. In asbestosis the fibrosis is diffuse or patchy but never nodular, and it is always more marked towards the bases of the lungs than elsewhere. In silicosis the upper portions of both upper and lower lobes are most frequently affected. In asbestosis, when a long interval of time has elapsed since exposure to the dust, the affected portions of the lung become sharply demarcated from adjacent comparatively healthy portions, but they never assume a nodular character. Bronchiectasis, often advanced and complicated by suppuration, is frequent in long-standing and severe cases of asbestosis: it is rare in silicosis, even when advanced. I attribute the difference in distribution of the lesions to the very different physical characters of the two dusts. The finely particulate silicious dusts are capable of being inhaled right into the bronchioles and no doubt some of the dust reaches the lung alveoli themselves. Asbestos dust is composed of sharp-pointed fibres of varying and often very considerable length—up to 100μ or more. They are much more likely to become stuck in the lumen of the bronchioles, or even to engage, by their sharp-pointed ends, in bronchi of larger size. Ultimately such fibres are likely to gravitate downwards to the bases, especially of the lower lobes, while far fewer are carried, by inhalation, into the apical regions, especially of the upper lobes.

Mechanical transportation by phagocytes is also very different in the two cases. It is easy for alveolar phagocytes to take up a charge of silicious particles, to transport it into the lung substance, and then to carry it, via the lymphatic channels, to the regional and even more distant lymph glands. The result in many cases, as already mentioned, is the development of a true silicotic lesion within the lymphatic glands themselves, most frequently the hilar and tracheobronchial, occasionally those of the upper abdomen. Transportation of asbestos fibres is a very different matter. While short fibres and short asbestos bodies are often engulfed in mononuclear phagocytes capable of movement and migration, it is much more usual to see large multinucleated giant cells, probably non-motile, with these structures in their interior. Yet in spite of the enormous number of asbestos fibres and bodies present within the lungs, it is only very exceptionally and in very small numbers that one sees them in the hilar or other lymph glands, and I am not aware that any lesion resulting from their presence has ever been described outside the lungs and pleura.

The diagnostic significance of asbestos bodies in the sputum.—Asbestos bodies probably make their appearance sooner or later in the sputum of all persons exposed for any length of time (weeks to months) to an atmosphere containing asbestos dust. In a case reported by Simson and Strachan (1931) they were present after only five months' exposure and I have found them in the sputum of persons whose occupation entailed only their occasional presence in the asbestos factory. It would seem that the sputum must come from the lung itself, or from the bronchioles at least, and usually the bodies are only demonstrable after the use of a concentration method and when the patient has a bronchitic attack or "chest cold". The presence of bodies as such in the sputum merely indicates that asbestos dust has been inhaled and has remained *in situ* for at least two or three months. It does as frequently affected as men and there is usually no history of the person having been engaged in an industry with a recognized silicosis risk. They have inhaled the dust from their "normal" environment and it has done them little harm. As a rule they are advanced in years. In persons employed (or who have formerly been employed) in "silicosis" industries, similar "subclinical" lesions are not infrequently encountered at autopsy and it is undesirable that undue significance should be attached to these findings in assessing claims for compensation. Naturally there are all intermediate grades between this strictly localized type of lesion and a full-blown silicosis with nodular or confluent lesions scattered throughout the parenchyma of the lungs.

In compensation cases, more importance should, however, be assigned to the presence of minimal (subclinical) silicotic lesions if these are accompanied by pulmonary tuberculosis, but in my experience this association is an infrequent one.

The silicotic apical scar.—For years it has been generally accepted (and supported by high authority) that virtually all apical scars are the result of old tuberculous disease. This view has always been challenged by a small number of observers, but it has remained for Davson and Susman (1937) and Davson (1939) to produce the final proof that the vast majority of these scars are silicotic and not tuberculous. In a series of 94 consecutive autopsies at all ages (excluding cases of gross pulmonary disease) there were 40 cases with apical scars which showed no histological evidence of healed tuberculosis and only 6 which did. A definite relationship was shown to exist between silicious dust accumulation in the upper part of the lungs and the presence of these non-tuberculous scars. Moreover frank silicotic nodules in various stages of development were demonstrated in 13 of these 40 cases, all of them belonging to the later age-groups in whom there was a high silica content in the lungs generally. The chief feature of the morbid histology of these non-tuberculous (silicotic) scars was the existence of an unbroken network of proliferated elastic fibres corresponding to the original pattern of the lung alveoli. The tuberculous scars, on the other hand, presented definite evidence of healed or quiescent tuberculosis, with one or more necrotic areas showing varying amounts of calcification, in all cases surrounded by a well-defined fibrous capsule. These caseous or calcified areas were devoid of any elastic network, indicating that there had been a breakdown of lung structure of a kind not seen in the purely silicotic type of scar. Davson has produced additional histological evidence for the non-tuberculous character of the vast majority of apical scars.

In fact, it is usually quite easy to distinguish the two types of scar by the naked eye. Purely silicotic scars are nearly always flat and superficial, but may be, superficially, quite extensive, and they are often covered by a plaque of hyaloserositis. On section they are black, grey-black or blue-black in colour, with a sharply-defined deeper margin. They range from 1 or 2 mm. to about 1 cm. in thickness and the cut surface is usually homogeneous. There are no contained foci of caseation or calcification. Pleural adhesions are usually lacking, and when present are by no means dense. These silicotic scars start at quite an early age and continue to enlarge with the passage of time. Like the other subclinical forms of silicosis already described they are no doubt due to the inhalation of road dust and silicious ash from domestic and industrial fires.

Silicosis of the spleen.—Classical nodular silicosis of the spleen is rare. It is probably due in most cases to a silicotic gland or glands ulcerating through into a branch of the pulmonary artery or vein (cf. Heggie, 1946). It can therefore occur in cases of glandular (subclinical) silicosis as well as in cases of gross pulmonary disease. Indeed the only case which I have seen was of this kind. There was gross glandular silicosis in both mediastinum and upper abdomen, but the lungs were hardly affected. The cause of death was congestive heart failure with great cardiac hypertrophy, apparently due to intense indurative mediastinitis with complete obliteration of the pericardium and both pleural sacs. To this the glandular silicosis may well have contributed, but there was evidence also of old rheumatic valvular disease, although without serious mechanical defect.

PULMONARY ASBESTOSIS

The contrast between silicosis and asbestosis in respect of the character and distribution of the lesions is now well established. In asbestosis the fibrosis is diffuse or patchy but never nodular, and it is always more marked towards the bases of the lungs than elsewhere. In silicosis the upper portions of both upper and lower lobes are most frequently affected. In asbestosis, when a long interval of time has elapsed since exposure to the dust, the affected portions of the lung become sharply demarcated from adjacent comparatively healthy portions, but they never assume a nodular character. Bronchiectasis, often advanced and complicated by suppuration, is frequent in long-standing and severe cases of asbestosis: it is rare in silicosis, even when advanced. I attribute the difference in distribution of the lesions to the very different physical characters of the two dusts. The finely particulate silicious dusts are capable of being inhaled right into the bronchioles and no doubt some of the dust reaches the lung alveoli themselves. Asbestos dust is composed of sharp-pointed fibres of varying and often very considerable length—up to 100μ or more. They are much more likely to become stuck in the lumen of the bronchioles, or even to engage, by their sharp-pointed ends, in bronchi of larger size. Ultimately such fibres are likely to gravitate downwards to the bases, especially of the lower lobes, while far fewer are carried, by inhalation, into the apical regions, especially of the upper lobes.

Mechanical transportation by phagocytes is also very different in the two cases. It is easy for alveolar phagocytes to take up a charge of silicious particles, to transport it into the lung substance, and then to carry it, via the lymphatic channels, to the regional and even more distant lymph glands. The result in many cases, as already mentioned, is the development of a true silicotic lesion within the lymphatic glands themselves, most frequently the hilar and tracheobronchial, occasionally those of the upper abdomen. Transportation of asbestos fibres is a very different matter. While short fibres and short asbestos bodies are often engulfed in mononuclear phagocytes capable of movement and migration, it is much more usual to see large multinucleated giant cells, probably non-motile, with these structures in their interior. Yet in spite of the enormous number of asbestos fibres and bodies present within the lungs, it is only very exceptionally and in very small numbers that one sees them in the hilar or other lymph glands, and I am not aware that any lesion resulting from their presence has ever been described outside the lungs and pleura.

The diagnostic significance of asbestos bodies in the sputum.—Asbestos bodies probably make their appearance sooner or later in the sputum of all persons exposed for any length of time (weeks to months) to an atmosphere containing asbestos dust. In a case reported by Simson and Strachan (1931) they were present after only five months' exposure and I have found them in the sputum of persons whose occupation entailed only their occasional presence in the asbestos factory. It would seem that the sputum must come from the lung itself, or from the bronchioles at least, and usually the bodies are only demonstrable after the use of a concentration method and when the patient has a bronchitic attack or "chest cold". The presence of bodies as such in the sputum merely indicates that asbestos dust has been inhaled and has remained *in situ* for at least two or three months. It does not necessarily mean that a fibrotic process is already in existence or that asbestosis will ultimately develop. Concentration of dust as well as length of exposure must be taken into account: probably it is the more important. It remains to be seen just how effective are the elaborate preventive measures now in use in the factories, but I must point out that all the fatal cases I have seen were those of persons who had been employed in asbestos manufacture for at least part of their working time prior to the introduction of these modern preventive measures.

The finding of "clumps" of asbestos bodies in the sputum is a very different matter (Stewart, Tattersall and Haddow, 1932; Page, 1935). In order that such clumps may escape from the parenchyma of the lung it is necessary that the alveolar walls should be broken down, either by a simple suppurative (bronchopneumonic) process or by tubercle. The former is the more likely, as tuberculous caseation not only causes the clumps to disintegrate but also leads to absorptive changes in the bodies themselves. Clumps must be searched for with care and a concentration method should be used (Stewart, 1929, 1934), but not too vigorously lest the clumps be broken down. I have now found clumps in the sputum in nearly a dozen cases and am satisfied that their presence is tantamount to a diagnosis of asbestosis. By this time, it must be admitted, it is probable that the clinical and radiological picture is already diagnostic, and the search for clumps a work of supererogation. The presence of single bodies in large numbers, especially if they are large, deeply pigmented and much "weathered", is at least suggestive and confirmatory.

Finally I would record the opinion that asbestosis is a more serious disease than silicosis. Even a short period of exposure (six months for example) to a dust of sufficient concentration may lead to a progressive fibrotic process which will ultimately kill the patient, it may be after an interval of many years. There can be no doubt, however, that modern protective methods are very effective in minimizing the occupational risk, and much credit is due to Dr. Merewether for his pioneer investigations into this sinister and insidious disease and its prevention.

REFERENCES

DAVSON, J. (1939) *J. Path. Bact.*, 49, 483.
——, and SUSMAN, W. (1937) *J. Path. Bact.*, 45, 597.
HEGGIE, J. F. (1946) *J. Path. Bact.*, 58, 575.
PAGE, R. C. (1935) *Amer. J. med. Sci.*, 189, 44.
SIMSON, F. W., and STRACHAN, A. S. (1931) *J. Path. Bact.*, 34, 1.
STEWART, M. J. (1929) *Brit. med. J.* (ii), 581.
—— (1934) *J. Tech. Meth. and Bull. Internat. Assoc. Med. Museums*, 13, 70.
——, TATTERSALL, N., and HADDOW, A. C. (1932) *J. Path. Bact.*, 35, 737.

Section of Radiology

President—WHATELY DAVIDSON, M.D., F.R.C.P., F.F.R.

[*March* 21, 1947]

Some Experiences with Bone Tumours. [*Abridged*]

By JAMES F. BRAILSFORD, M.D., PH.D., F.R.C.P., F.I.C.S.

Radiologist, The Royal Cripples and The Queen Elizabeth Hospitals, Birmingham

THERE is probably no more interesting or varied study in pathology than the study of bone tumours. Throughout the years there has been a constant search by clinicians, pathologists and more recently radiologists to find evidence which would reveal the nature of these lesions. Much has been learnt which permits us to classify the majority of bone tumours; but with one's experience limited to a little less than forty years—which includes the macroscopic and microscopic study of pathological conditions in the food animals at the Birmingham Public Abattoir for over nine years—I have to admit that we have not yet discovered one sign on which we can entirely depend for a solution of our difficulties. We have learnt that the clinical features can be indistinguishable, though the tumours are essentially different, even as regards their simplicity and malignancy; they may appear to be grave yet the lesion simple; they may appear insignificant yet the lesion may be deadly.

Because it was felt that early diagnosis and prompt amputation gave the best chance to eradicate malignant disease, undue significance and reliance have been placed upon the interpretation of the histological appearances of the tumour tissue, and biopsy became, and in some centres still is, the recognized initial measure in treatment. Alas, because pathology was taught from well-established lesions which presented certain well-defined characters, the impression was conveyed to surgeons that biopsy afforded the best evidence. But those who have had a wide experience know that the most simple lesions can contain cellular tissues which are indistinguishable from some considered as characteristic of malignancy; though in some highly malignant tumours those characters may not be found. Hence, from a given tumour, material has been submitted to a number of expert pathologists and as many different opinions have been obtained, ranging from simplicity to high malignancy. The more extensive the histological investigations throughout the course of a bone tumour, the more varied and confusing the opinions of the different observers appear to be. On the other hand, individual histologists have seen the same cellular structures in groups of tumours which they have classified accordingly, though these tumours have been proved clinically and radiologically to be of essentially different pathology. No better examples of this can be seen than those two cases illustrated on pages 192 (fig. 125) and 193 (fig. 126) in Geschickter and Copeland's "Tumors of Bone" 1936 [1]. Both tumours are recorded as being chondroblastic sarcoma from their histological appearances, yet the radiographic definition of the tumour tissue in fig. 125 suggests simplicity which is borne out by the subsequent cure, whereas fig. 126 shows that the bone structure has been reduced to a "mush", as one would expect from the irregular destruction by invasion of malignant cells and this is borne out by the subsequent fatal issue.

To-day with the ubiquity of X-ray units the radiograph has become the first court of reference. This court also has its great limitations and difficulties which are all too little appreciated. As in pathology, so in radiology, the teaching of clinicians has been from spectacular and well-established radiographic appearances while the more common slight and insidious changes, because more difficult to appreciate by any but the experienced observers, have been avoided.

Because the radiographs of lesions show spectacular localized irregularities in calcification and ossification such lesions are thoughtlessly dubbed sarcomata, and sometimes it is not until irrevocable and unnecessary amputation has been performed, and the subsequent history has indicated the useless disaster, that the cases have been published as "—— simulating sarcoma". The literature contains records of many such cases. Amputations have been performed because of a mass of callus at the site of an unrecognized fracture, localized myositis ossificans, subperiosteal hæmatomata, and hæmatomata associated with neurotropic lesions, scurvy, osteogenesis imperfecta, hæmophilia, &c.

The admonishing words of John Hunter, "It is astonishing to see what little curiosity people have to observe the operations of nature and how very curious they are about the operations of art", deserve to be especially emphasized in the diagnosis and treatment of bone tumours. Radiology has given the clinician a further means of observing the not necessarily mean that a fibrotic process is already in existence or that asbestosis will ultimately develop. Concentration of dust as well as length of exposure must be taken into account: probably it is the more important. It remains to be seen just how effective are the elaborate preventive measures now in use in the factories, but I must point out that all the fatal cases I have seen were those of persons who had been employed in asbestos manufacture for at least part of their working time prior to the introduction of these modern preventive measures.

The finding of "clumps" of asbestos bodies in the sputum is a very different matter (Stewart, Tattersall and Haddow, 1932; Page, 1935). In order that such clumps may escape from the parenchyma of the lung it is necessary that the alveolar walls should be broken down, either by a simple suppurative (bronchopneumonic) process or by tubercle. The former is the more likely, as tuberculous caseation not only causes the clumps to disintegrate but also leads to absorptive changes in the bodies themselves. Clumps must be searched for with care and a concentration method should be used (Stewart, 1929, 1934), but not too vigorously lest the clumps be broken down. I have now found clumps in the sputum in nearly a dozen cases and am satisfied that their presence is tantamount to a diagnosis of asbestosis. By this time, it must be admitted, it is probable that the clinical and radiological picture is already diagnostic, and the search for clumps a work of supererogation. The presence of single bodies in large numbers, especially if they are large, deeply pigmented and much "weathered", is at least suggestive and confirmatory.

Finally I would record the opinion that asbestosis is a more serious disease than silicosis. Even a short period of exposure (six months for example) to a dust of sufficient concentration may lead to a progressive fibrotic process which will ultimately kill the patient, it may be after an interval of many years. There can be no doubt, however, that modern protective methods are very effective in minimizing the occupational risk, and much credit is due to Dr. Merewether for his pioneer investigations into this sinister and insidious disease and its prevention.

REFERENCES

DAVSON, J. (1939) *J. Path. Bact.*, 49, 483.
——, and SUSMAN, W. (1937) *J. Path. Bact.*, 45, 597.
HEGGIE, J. F. (1946) *J. Path. Bact.*, 58, 575.
PAGE, R. C. (1935) *Amer. J. med. Sci.*, 189, 44.
SIMSON, F. W., and STRACHAN, A. S. (1931) *J. Path. Bact.*, 34, 1.
STEWART, M. J. (1929) *Brit. med. J.* (ii), 581.
—— (1934) *J. Tech. Meth. and Bull. Internat. Assoc. Med. Museums*, 13, 70.
——, TATTERSALL, N., and HADDOW, A. C. (1932) *J. Path. Bact.*, 35, 737.

behaviour of bone tumours, and though it has the advantage recognized by the lay and medical press of 1896, immediately Roentgen's discovery was made known, i.e. that the examination can be made without causing the patient any additional pain, it has been neglected. One radiographic examination may give the required evidence for diagnosis, but in many cases it is insufficient for this purpose, and, like the clinical examination, must be repeated, sometimes frequently, over a course of months, before we can determine the nature of the lesion.

In previous papers [2] I have drawn attention to the importance of the latent negative radiographic period which elapses between the onset of clinical signs and symptoms and the development of sufficient changes for radiographic demonstration, and the positive radiographic symptomless period during which there may be spectacular radiographic evidence of healed lesions which are of no clinical significance. As an instance of the significance of the former we may take metastatic carcinoma where the clinical signs and symptoms may be present at a site months before radiographs indicate characteristic changes in the bone. As an instance of the latter—the positive radiographic symptomless period—we have no better example than the aseptic infarct in bone which occurs without recognition and is not discovered until a radiograph of the part is taken because of some other factor, i.e. trauma, arthritis; then undue significance may be placed upon the spectacular radiographic appearances, and biopsy with its erroneous histological interpretation is sometimes followed by unnecessary amputation. Failure to seek the co-operation of the radiologist is responsible for many errors and any registry of bone tumours which fails to recognize that expert radiographic evidence is an essential complement to that obtained by the clinician and pathologist will fail to achieve the best results; indeed, it may give rise to erroneous impressions.

There is perhaps no better instance of the confusion which can arise from interpretations of extensive histological examinations in the case of a simple lesion with prominent clinical signs and ill-understood spectacular radiographic appearances than that recorded by S. L. Baker [3]. In this case of osteogenesis imperfecta, the child sustained a fracture and at the site an extensive hæmorrhage occurred which produced clinical and radiographic signs interpreted as those of a rapidly growing sarcoma. A biopsy was performed five weeks after the fracture and "disarticulation of the hip was considered but regarded as too risky and of doubtful value and palliative X-ray treatment was decided on". A course of deep X-radiation was given. The first biopsy yielded material which "I considered showed a chondrosarcoma but later had expressed doubt upon, considering that the extreme rarity of a sarcoma developing on fracture indicated further investigation of the biopsy material". A second biopsy yielded material which favoured a better outlook, and clinical and

Fig. 1a.—Radiograph, December 28, 1944, of arm of girl, M. W., aged 14 years, with the history of an injury seven weeks previously, showing multiple linear accretions on upper third of the humerus with some alteration in the internal structure, surrounded by a massive fusiform swelling of the soft tissues. Clinically diagnosed as a Ewing's sarcoma. Found to have a positive Wassermann.

Fig. 1b.—Radiograph of M.W., October 1, 1946, after sulphathiazole and antisyphilitic medication —complete resolution.

It is very rare for trauma to be followed at once by the development of sarcomatous metaplasia. The history of trauma is often given in cases of sarcoma, but radiographs taken immediately after the alleged trauma indicate that the lesion was well developed at the time of the trauma, which, because of abnormal tenderness, drew the patient's attention to the site. A knowledge of the time taken for the sequence of radiographic changes to have developed supported the view that the trauma was the cause of the lesion.

In some cases sarcomatous metaplasia occurs at the site of a known old fracture or lesion in the bone. The radiographs will indicate, however, to the trained observer that the bone lesion is old, but it may not, in the early stages, show any evidence that malignancy has developed. It is the clinical evidence in these cases which should guide us.

Fig. 2a.—Radiograph of fusiform swelling of upper arm of B.W., aged 6 years, November 1944, showing disintegration of the upper half of the humeral shaft periosteal cuff and multiple lesions in the lungs.

Fig. 2b.—Radiograph of B. W., January 4, 1945, showing marked increase in the lung lesions. Diagnosed as sarcoma with multiple secondaries in the lungs. All lesions completely resolved within a few months and patient now quite fit. The only medication—a course of sulphathiazole.

The nature of the condition must be one of conjecture. Even for an osteomyelitis (of which she gave no clinical or laboratory evidence) with multiple pulmonary infarcts, the cure is very remarkable, for neither the bone nor the lung, which were both seriously affected, showed any residual lesion—a rarity with such disintegration. It is possible that the condition was related to that group of bone pathology, the granulomata of reticulo-endotheliosis which includes xanthomatosis, lipoid granuloma, eosinophil granuloma, or possibly to some such infection as parathyroid, for lesions in this group may heal without leaving any scars. As I have indicated elsewhere [8] aborted osteomyelitis from any cause may be associated with radiographic appearances liable to be mistaken for sarcoma. A remarkable and complete cure resulted in this case without any surgical intervention.

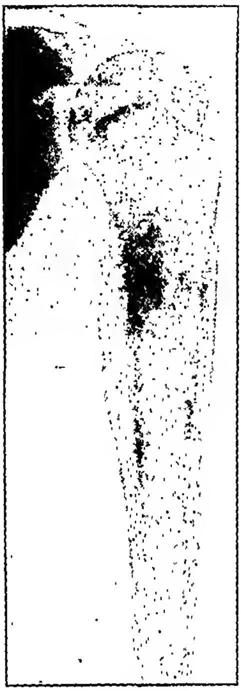


FIG. 1A

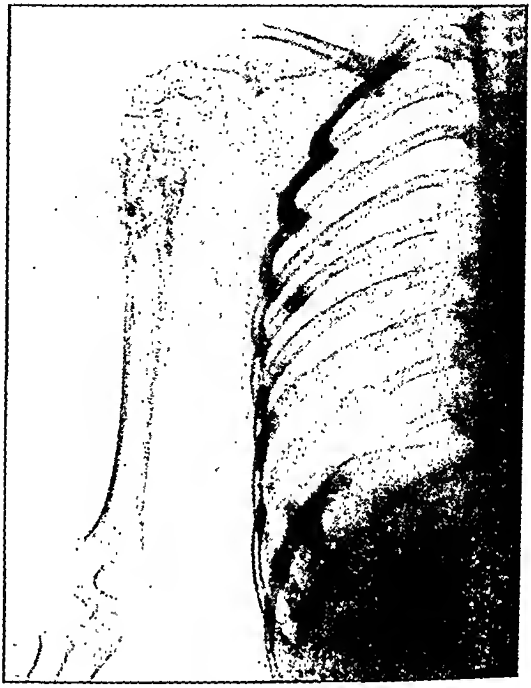


FIG. 2A

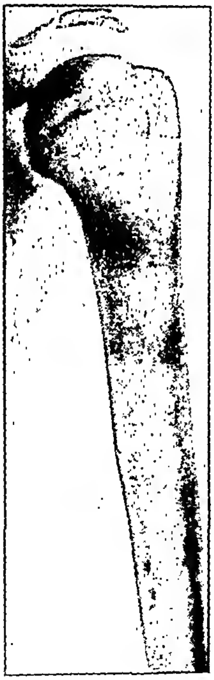


FIG. 1B

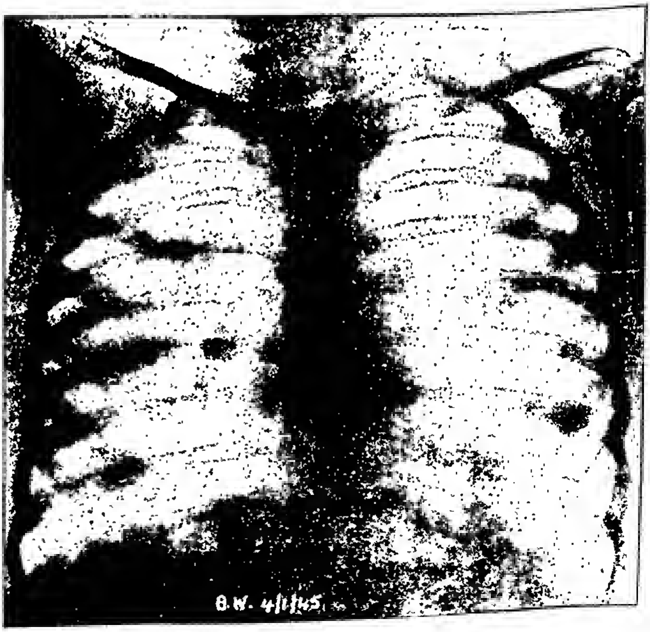


FIG. 2B

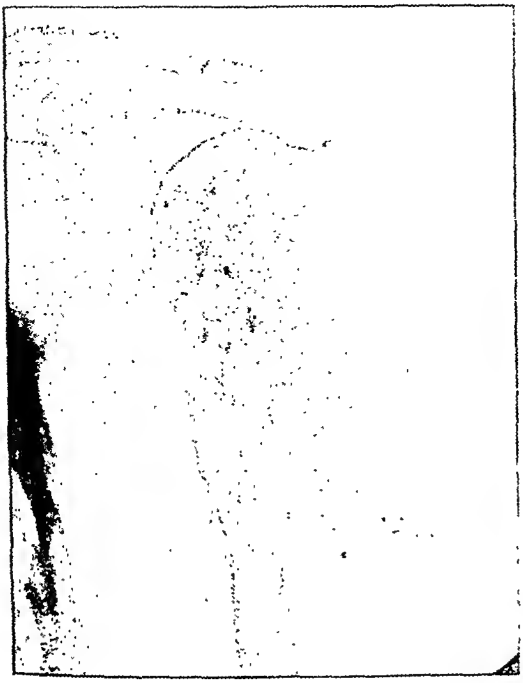


FIG. 3A

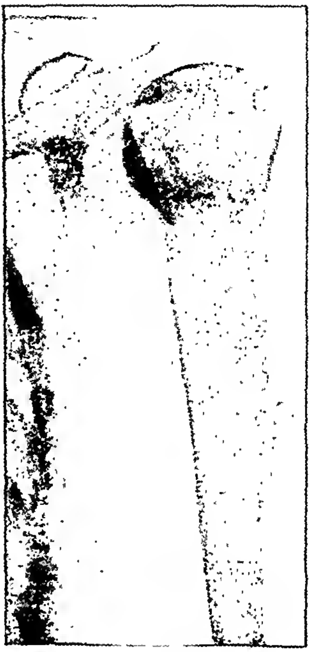


FIG. 3B

FIG. 3A.—Radiograph October 27, 1938, of fusiform swelling of arm of girl aged 18 years showing disintegration of upper third of the humerus.

FIG. 3B.—Radiograph of same case, fig. 3A, October 4, 1940 (1,274 r had been given in the interval), showing complete resolution, which has persisted.

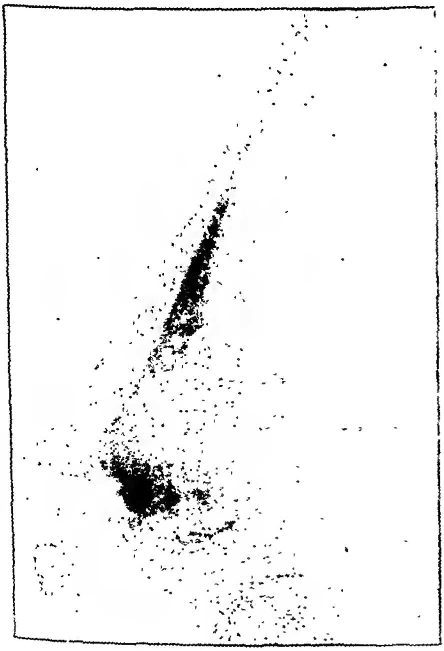


FIG. 4A

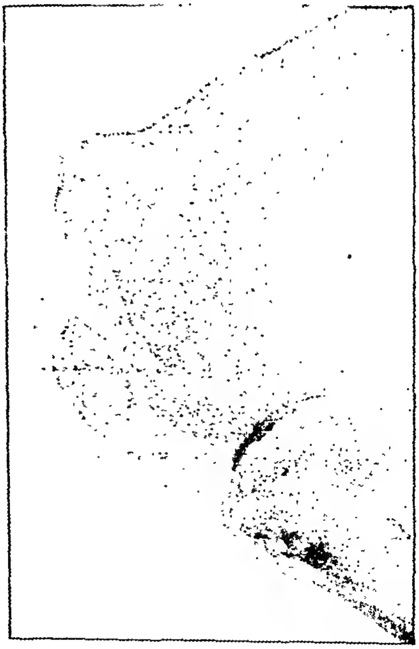


FIG. 4B

radiographic observations over three years confirmed this. But as I had indicated in a previous paper [4], to which S. L. Baker referred, the nature of such lesions, their development, and even their essential histological features may be determined by serial radiographic examinations which cause the patient no pain and do not involve the risk of the erroneous interpretation which might have cost this patient useless pain and risk of losing the affected limb. As I recorded, such a lesion in a patient with osteogenesis imperfecta did eventually develop malignant metaplasia, with the spread of metastases and death; but this event has been seen to occur in isolated cases with localized or generalized osseous dysplasia but is not the common sequence.

When we consider the answer to the question, What is a bone tumour? we must use some classification of the lesions which appear clinically, histologically and radiographically to fall under that heading. As I have indicated in a previous paper [5] classification of bone tumours on clinical signs and symptoms alone is impossible. Classification on clinical and histological grounds together is likely to be erroneous as already indicated, and must be based essentially on post-mortem and histological appearances rather than on living tissue. Modern classification is being made principally on radiographic findings, though, as indicated, this must be made with recognition of possible shortcomings. By radiography alone can we study the living structure of the tumour, watch its development, life-history and the reaction of the adjacent tissues; but in our interpretation we must always keep a careful scrutiny of the clinical course. The radiography must always be first-class showing the intimate osseous structure in sharp definition with the lesion in the middle of the radiograph so that its extension and changes can be compared with subsequent radiographs. Anything less than this is unsatisfactory and may seriously affect the interpretation.

By radiography we can separate the bone tumours into the following seven sections: (1) Congenital and developmental irregularities of the skeleton. (2) Dysplasias and dystrophies of bones. (3) The deficiency and blood diseases affecting the skeleton. (4) The secondary effects of trauma to bone. (5) Granulomata of bones. (6) Simple tumours of bones. (7) Malignant tumours of bones.

Briefly summarized, the essential features of lesions in these sections are as follows:

(1) *The Congenital and Developmental irregularities of the skeleton* can be recognized from the maturity of the osseous structure of the affected bones.

(2) *Dysplasias and dystrophies of the skeleton.*—The skeletal changes associated with these irregularities of mesoblastic growth may affect

(*a*) the whole skeleton as in: Osteogenesis imperfecta; Albers-Schönberg's disease; achondroplasia; chondro-osteo-dystrophy,

or

(*b*) while in isolated cases the dysplasia may be generalized throughout the skeleton, it is more frequently found to involve mainly one side of the skeleton; every bone on that side being completely involved, or bearing but single or multiple foci; the bones on the other side being free or exhibiting one or two small lesions.

The degree of the dysplasia may be such as is incompatible with life; it may permit of childbirth, the infant may come to adolescence or maturity; again, it may be so trivial that it is only discovered by radiography during examination following trauma, disease, &c. The recognition of such lesions may be of great significance.

Such dysplasias may be associated with:

(*a*) Proliferation of myxomatous tissue (polycystic dysplasia or osteitis fibrosa cystica).
(*b*) Proliferation of fibrous tissue (fibrosis of bone; polycystic fibrous dysplasia).
(*c*) Proliferation of angiomatous tissue (Kast's disease, &c.).
(*d*) Proliferation of chondrous tissue. (Ollier's disease, &c.).
(*e*) Proliferation of osseous tissue (multiple exostoses; Keith's diaphyseal aclasia).
(*f*) Proliferation of abnormal osseous tissue (Léri's melorheostosis).

These dysplasias may be associated with the deficiency diseases, &c., their appearances being accordingly changed.

The differential diagnosis includes such diseases as rickets, scurvy, hæmophilia, osteo-myelo-sclerosis (associated with polycythemia and subsequently anæmia and leukæmia), fluorosis, carcinomatosis, myelomatosis, hyperparathyroidism, Paget's disease.

FIG. 4A.—Radiograph, November 28, 1944, of painless and much swollen leg of a boy aged 14 years, showing a fracture dislocation through the femoral diaphysio-epiphyseal junction and multiple linear accretions on the lower half of the diaphysis, detached bony fragments and calcium deposits in the soft tissues. Amputation avoided because of paralysis of extremities associated with spina bifida.

FIG. 4B.—Radiograph, May 24, 1946, showing complete resolution of the lesion. No treatment of any description in the interval.

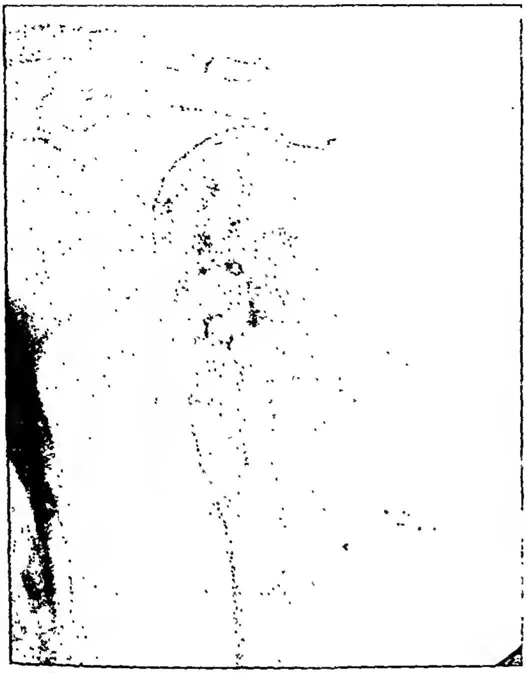


FIG. 3A

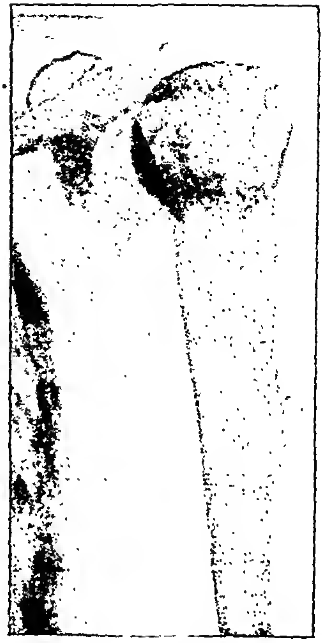


FIG. 3B

FIG. 3A.—Radiograph October 27, 1938, of fusiform swelling of arm of girl aged 18 years showing disintegration of upper third of the humerus.

FIG. 3B.—Radiograph of same case, fig. 3A, October 4, 1940 (1,274 r had been given in the interval), showing complete resolution, which has persisted.

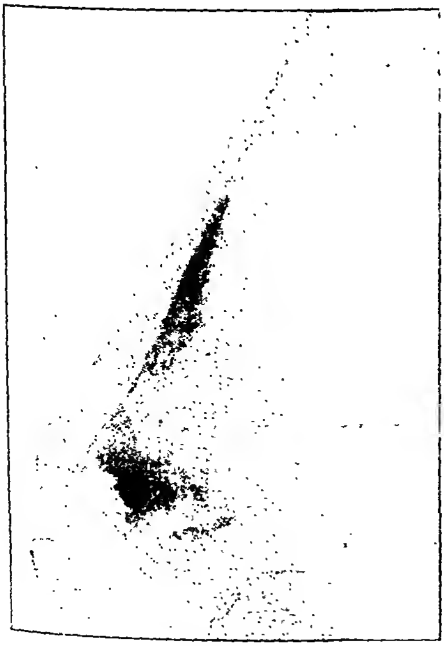


FIG. 4A

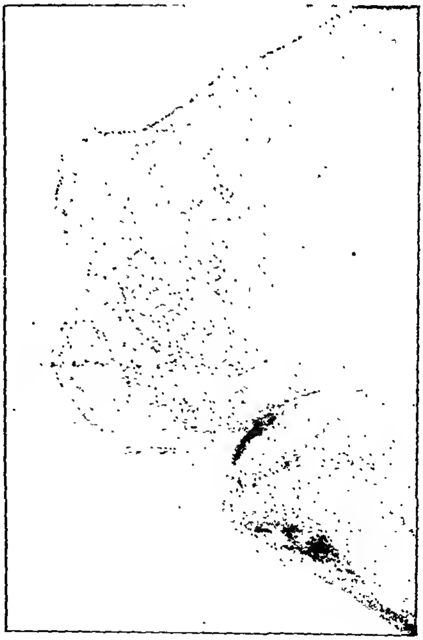


FIG. 4B

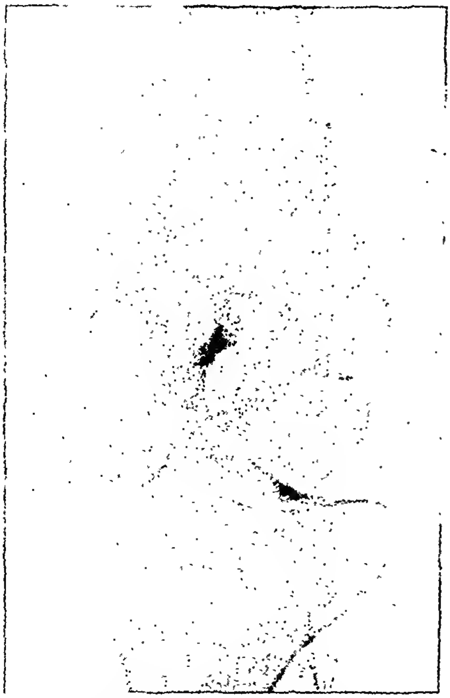


FIG. 5A.—Radiograph of M. H., aged 20 years, August 15, 1945. Osteoclastoma.

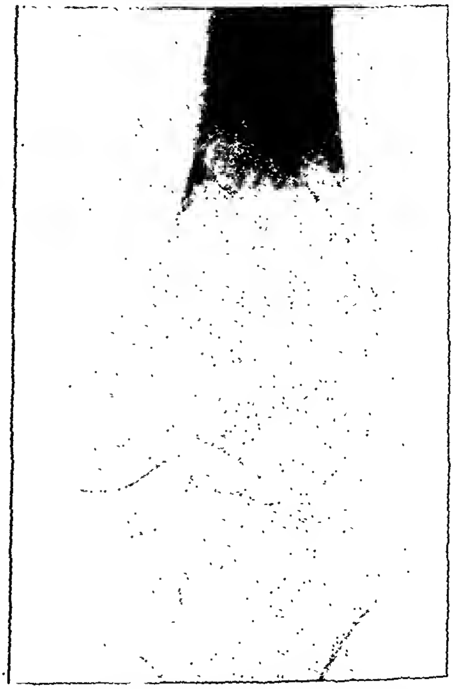


FIG. 5B.—Radiograph of M. H., September 23, 1946, after X-radiation therapy.

FIG. 5A and 5B.—This case illustrates an osteoclastoma which responded with the known sequence of changes following X-radiation therapy, i.e. for a month or so progressive decalcification, destruction of bone in and around the tumour site, followed by gradual recalcification and consolidation, and—if the limb has been carefully immobilized during the osteolytic phase—without any deformity. No biopsy was performed, there has been no sign of secondaries and the limb is sufficiently consolidated to permit of normal function.

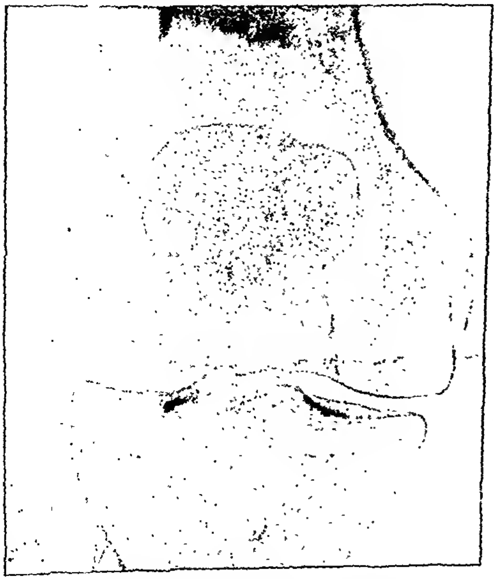


FIG. 6A

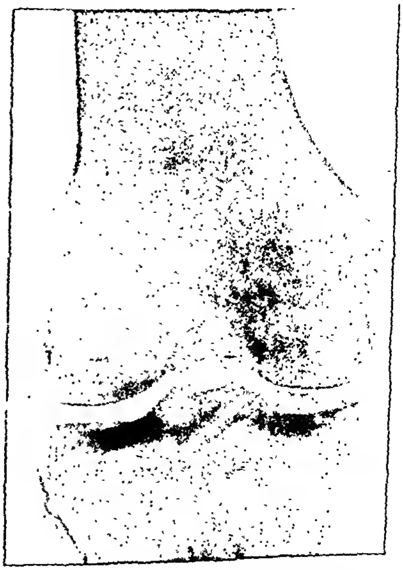


FIG. 6B

FIG. 6A.—Radiograph of R. M., aged 31 years. July 1944. Diagnosed osteoclastoma on radiographic appearances. FIG. 6B.—Radiograph, January 1, 1945. Failure to respond to repeated courses of deep X-radiation—amputation because of hæmorrhage—histology typical osteoclastoma. No recurrence to this date (November 1947) and patient in good health.

(3) *The deficiency and blood diseases affecting the skeleton.*—The characteristic clinical and radiographic features of fœtal, infantile, resistant or late rickets, renal rickets, osteomalacia, idiopathic steatorrhœa. Dislocations, fractures, healing deformities.

Scurvy: Subperiosteal hæmorrhages. Dislocations. Tumours associated with osteogenesis imperfecta.

Hæmophilia: Tumours simulating sarcoma. Joint changes.

Polycythemia, Anæmias and Leukæmias: General skeletal changes. Osteo-myelosclerosis. Localized foci.

(4) *The secondary effects of trauma on bone* in which we must consider: (*a*) the time factor in production of changes, (*b*) the latent negative radiographic period and the positive radiographic symptomless period, (*c*) overlap of these periods.

Acute atrophy of bone: Myositis ossificans. Conflicting histology. Treatment.

Avascular necrosis: Time factor very important for detection. Secondary effects. Joint changes. Plasticity of bones. Secondary inflammatory and neoplastic changes. Frequency.

(5) *Granulomata of bone.*—Time factor in the production of clinical and radiographic signs. The latent negative and positive radiographic periods. Changes produced in bones by different organisms—the rate of change at different ages—the degree of resolution at different ages.

Pyogenic organisms: The typhoid group.

Brodie's abscess: Differential diagnosis.

Osteoid osteoma: A granuloma with much surrounding reaction.

Tuberculosis of bones and joints: Characters of rate of development and healing. Abscess features. Frequency of pulmonary tuberculosis—type.

Syphilis of bone: Characters at different ages. Resemblance to other lesions—sarcoma, &c.

Eosinophilic granuloma: Characters—response to treatment.

Lipoidgranulomatosis: Hand-Schüller-Christian syndrome. Result of treatment. Letterer-Siwe's disease.

Lymphogranulomatosis: Bone changes in.

(6) *Simple tumours of bone and adjacent tissues.*—Lipoma, myxoma, fibroma, angioma, chondroma, osteoma and osteoclastoma, have characteristic radiographic appearances. Localized resection offers the best cure. Secondary malignant metaplasia may develop. Effect of radiation.

(7) *Malignant tumours of bone.*—The clinical features and the time factor show considerable variation.

Consideration of the 10 radiographic features [6] which are associated with malignancy. The importance of the clinical history and the value of biopsy.

Within the limits of this paper it is impossible to illustrate examples of lesions in all these sections. That has been done elsewhere [6], but the following figures illustrate a few of the many cases which were watched throughout their course, during which they exhibited features liable to be misinterpreted as indicating malignancy, yet which resolved without any surgical intervention. In some (as in the case described by S. L. Baker) major surgical measures would undoubtedly have been performed, but for other features in the cases which indicated the futility of such actions.

CONCLUSION

For the diagnosis of tumours of bones we are dependent on the clinical and radiographical evidence. This can be obtained without causing the patient any pain and without disturbing the lesion. Such evidence permits of the most accurate diagnosis. In many cases the radiographic evidence in itself is distinctive and permits accurate diagnosis at a time when the clinical examination yields little or no contribution. The values of the two methods are reversed when the lesion does not involve the bone. In some cases neither the clinical nor the radiographical evidence is sufficiently characteristic at the first examination. We may have to make repeated observations over several weeks or months before we can decide. Because it was thought that prompt amputation of the affected limb offered the best and only cure and that the waiting period could be eliminated by histological examination of the tumour tissue, a resort to biopsy was often made. I regret to say that in my experience when the clinical and the radiographic evidence is indefinite the histological appearances are at least equally indefinite—in fact may only add confusion or errors to the judgment. The cases of two young women under 20 years of age occur to me. Both of them had lesions in the lower third of the humerus. The one appeared radiographically as a localized rounded sequestrum within a cyst; it appeared to be a simple lesion. The sequestrum was enucleated and some sections were histologically examined and reported as showing evidence of a rapidly growing sarcoma. The limb was amputated but on careful examination of the specimen it had all the aspects of simplicity, though one section had the suspicious cells. The patient is now alive and fit ten years later. The second patient had an ill-defined change in the shaft, the appearance of which suggested an early Ewing's tumour, but clinically it appeared to be a localized inflammatory lesion. Some pus-like material was evacuated by the surgeon but histological examination of small pieces of tissue from the site were reported as having the characters of a highly malignant endothelial myeloma, and as at that time prompt amputation was regarded as the only chance of cure, I urged that this should be done. Fortunately the parents refused, for the lesion completely resolved, and now, ten years after, she is fit and well.

I have not been fortunate enough to see cure resulting from prompt amputation of a limb showing the typical radiographic evidence of an osteogenic sarcoma. To amputate a limb when the radiographic and clinical evidence is not conclusive, even though the histology suggests malignant disease, is to take an unjustifiable risk. If biopsy is excusable, it is so when it provides material which supports the clinical and radiographic evidence of simplicity, rather than malignancy, and prevents amputation. This raises the question as to who shall interpret the radiographic appearances. My answer is, the person who by learning and practice has fitted himself to do so. There is a growing tendency for the clinician to use his own interpretation of radiographs rather than that of his colleague, the radiologist. This is unfortunately the cause of much dissatisfaction. The clinician by co-operation can bring forth evidence which permits of great improvement in the value of the radiologist's report. Much of my own radiological interpretation I have learnt with the help of co-operating clinicians, for in certain specialized fields the clinician has the better chance of correlating the clinical and surgical findings with the radiographic appearances; but he cannot do this to the best advantage unless he has made himself acquainted with all the radiographic features likely to influence the decisions. Unless the radiologist seeks the information which the clinician can give he will be unable to give that additional help which the clinician has a reasonable right to expect. The radiologist's opinion is sometimes ignored. The clinician may well excuse himself for being wrong in such cases, but he may not forgive the radiologist for being right, until he has learnt that the practice is consistent.

May I suggest to those concerned with the education and training of radiologists that the student be taught more extensive radiology in its application to clinical methods at the expense of the practically useless physics, which at present engages far too much of his time. Some of the responsible elders in radiology appear to believe that there is no need to give the student for his diploma examination more than a general outline of the common conditions met with in radiology. To-day the medical student is taught that, but I consider that the radiologist ought to make himself so familiar with all the radiological features which are met with in all specialities, that he can give expert advice to the consultant specialist seeking it. It should be his job to find out in what way radiology can help. He will only be able to do this if he is not compelled to acquire non-essential facts. A better knowledge of clinical medicine is far more important than a smattering of physics which he can safely leave to the physicist. The more radiographs I see the more significance I place on clinical findings.

A number of cases have reported at hospital complaining of pain, unusual tumour, tenderness, pulsation, or fracture of relatively short duration; radiographs of the affected area have shown evidence of osteogenic sarcoma, and radiographs of the chest have shown, even at the first examination, evidence of secondaries in the lung. Some patients without the latter evidence have been subjected to prompt amputation but metastases have subsequently developed with fatal issue.

Experience with these cases, and with those amputations of limbs for lesions which are subsequently found to be simple, indicates that there is nothing to be gained by undue haste and precipitate amputation but something can be gained by observation of the clinical features and serial radiographs; it supports the conclusions included in the final chapter of my book.

BIBLIOGRAPHY

1 Geschickter, C. F., and Copeland, M. M. (1936) Tumors of Bone, Rev. Ed., New York.
2 Brailsford, J. F. (1946) Evaluation of the Negative Radiological Report, *Practitioner*, **157**, 200.
3 Baker, S. L. (1946) Hyperplastic Callus Simulating Sarcoma in Two Cases of Fragilitas Ossium, *J. Path. Bact.*, **18**, 609.
4 Brailsford, J. F. (1943) Osteogenesis Imperfecta, *Brit. J. Radiol.*, **16**, 130.
5 —— (1946) Tumours of Bone, *Med. Pr.*, **216**, 399, 423.
6 —— (1947) Radiology of Bones and Joints, 4th Ed., London.
7 Szutu, C., and Hsieh, C. K. (1942) *Ann. Surg.*, **115**, 280.
8 Brailsford, J. F. (1946) Osteomyelitis Radiographically Resembling Sarcoma, *Lancet* (i), 498.
9 —— (1941) Changes in Bones, Joints and Soft Tissue Associated with Disease or Injury to the Central Nervous System, *Brit. J. Radiol.*, **14**, 320.
10 —— (1945) Sclerosing Sarcoma of Bone, *Brit. J. Radiol.*, **18**, 8.
11 —— (1943) Treatment of Osteoclastoma, *Lancet* (i), 776.
12 Speed, K. (1943) *Surg. Gynec. Obstet.*, **76**, 139.

Section of Urology

President—R. H. O. B. Robinson, F.R.C.S.

[*March* 27, 1947]

Injuries to the Bladder

By Richard A. Mogg, F.R.C.S.

The subject matter of this paper is the result of observations on a small series of cases treated at Naval Hospitals during the recent war.

Bladder injuries are seen more frequently during wartime, even then the incidence of these injuries is not high and in the 1914–18 war, Fullerton estimated that the incidence of bladder injuries in the B.E.F. casualties evacuated from France were not more than 1 : 3–4,000. On the other hand it is quite probable that the incidence of this injury, was higher than this, as the majority of bladder injuries are complicated by severe associated injuries from which the patients may die before they reach hospital or perhaps before a diagnosis can be made while in hospital.

There are two main types of bladder injury. The first is rupture, due to sudden increase of the internal hydrostatic pressure, and the second due to puncture or perforation from some foreign body or adjacent bone. With the exception of injuries sustained in wartime, rupture of the bladder is the more frequent of the major injuries of the bladder; occurring more often in males because of the greater hazard of exposure of the male to trauma. The injury is more frequently seen in the adult, but recent statistics from American surgeons have shown that the incidence in children is increasing, due, mainly, to the increased number of automobile accidents.

These injuries are nearly always complicated because the bladder is a well-protected viscus being entirely surrounded by bones, muscles and ligaments which constitute the pelvic girdle and it is only when it becomes distended that the apex of the bladder rises into the abdomen. It is then more vulnerable, not only because it lacks the protection of the pelvis, but because it now presents a larger target to the trauma-producing agent. Rupture of the distended bladder can result from comparatively slight trauma to the anterior abdominal bladder wall; this is especially seen in conditions that allow the bladder to become over-distended and the foremost of these is alcoholic intoxication. The diuretic effect of the alcohol fills the bladder allowing it to become overfilled and, combined with impairment of cerebration which prevents the anticipation of trauma, there is a lack of the normal protective function of the abdominal wall muscles for the bladder.

The anatomy of the pelvic fascia is the key to the subsequent pathological processes which occur following bladder injuries (figs. 1 and 2). Below the peritoneal attachments of the bladder, the vesical part of the visceral layer of the pelvic fascia completely invests the bladder, being loosely attached to it at the front and sides. It is the loose attachment of the fascia that allows the bladder to distend during the filling phase. This perivesical fascia can be definitely divided into two compartments, an anterior and a posterolateral, there being a free connexion between the two. The anterior or prevesical space can be readily

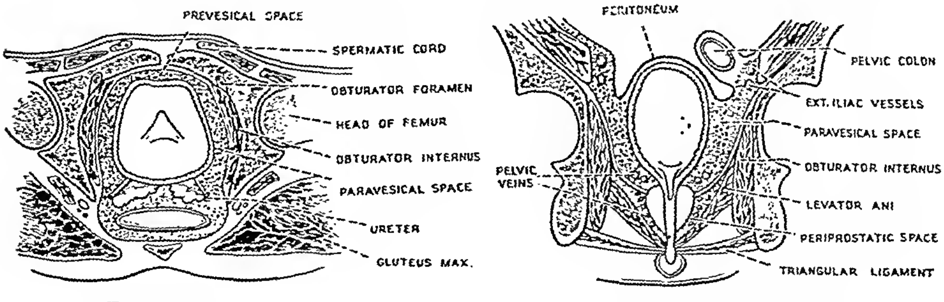


Fig. 1.—Transverse section

Fig. 2.—Vertical section.

Figs. 1 and 2.—Diagrams of perivesical cellular spaces at level of hip-joint. (From Sandrey and Mogg, *Lancet*, 1944 (i), 717.)

approached by the suprapubic route, by stripping the bladder from the front of the pubis. An effusion in this space presents in the suprapubic region and may be drained in this region, or it may track along the vas deferens and present in the inguinal region. If there is also damage to the pelvic girdle, the effusion may extend inferiorly along the obturator vessels and nerves deep to the origins of the adductor groups of muscles into the tissues of the thigh and counter-incisions in the inguinal and femoral regions may be needed to provide free drainage.

The posterolateral, or paravesical space, extends behind the bladder in front of the rectum communicating anteriorly with the prevesical space. It is immediately below the rectovesical pouch of the peritoneum and any effusion in it will gravitate between the bladder and the rectum and can be recognized on rectal examination as a diffuse boggy mass above the prostate gland. When the abdomen is opened in such a case, the rectovesical pouch in the male will be found to be diminished in depth by the underlying effusion. The posterolateral or paravesical space is best drained by the perineal route, which route provides dependent drainage.

The fascia in the perivesical spaces has very poor resistance to infection and any effusion into it, whether it be blood or urine, if allowed to remain, will rapidly suppurate. Records of the 1914-18 war showed that pelvic cellulitis was responsible for more deaths than any other single cause in patients who had suffered a bladder wound. It also plays a major part in the morbidity rate following bladder injuries and the late complications such as persistent cystitis, calculus formation, osteomyelitis of the pelvic girdle, infective arthritis of the hip-joint and ascending renal infection, result from a chronic perivesical cellulitis. Osteitis of the symphysis pubis is a common sequel of chronic perivesical cellulitis. Therefore, the most important factor in the treatment of any bladder wound is the prevention of perivesical cellulitis. This is achieved ideally by immediate suture of the wound or wounds of the bladder wall thereby preventing extravasation of urine and blood into the perivesical cellular tissue, and by adequate drainage of this cellular tissue. It is just as important to suture a bladder wound as it is to suture a wound of the gut. At the same time a diversion of the urine by suprapubic cystostomy will put the bladder at rest, prevent leakage of urine through the suture line and allow healing.

The types of injury to the bladder are varied in character and may range from extensive laceration with destruction of large areas of the bladder to contusions of the bladder wall. When the anterior abdominal wall is injured, the bladder may herniate through the wound, giving a condition described by Legueu as "L'extrophie traumatique". Small incisions or puncture wounds of the bladder are often difficult to find on operation, due to the fact that they seal themselves off quite readily but they can be seen on cystoscopy. A common type of wound is a through-and-through wound and a careful search should be made for the exit wound when the missile is not retained in the bladder. The most extensive injuries to the bladder are due to shell or bomb fragments which are low-velocity missiles and readily give rise to infection. Bullet wounds and bayonet stabs are usually clean perforations with little infection. Any missile which strikes the bony pelvis first will cause much soft tissue damage. The pubis, being compact bone, tends to splinter into small fragments when injured by missiles, these splinters being driven into the surrounding tissues ("Blessure à grand fracas", described by Legueu). As the sacrum and ilium are composed largely of cancellous bone, clear-cut perforations or fractures are produced when these are injured and bony fragmentation is far less than when the anterior part of the pelvic girdle is injured.

The track of the missile injuring the bladder is usually an oblique one and it was found by Fullerton that 75% of his cases had wounds in the buttock. Therefore any wound of the buttock should be regarded with suspicion and carefully investigated as soon as possible. Anteroposterior wounds are much less common. Other routes are via the thigh, the groin and the perineum.

Injuries of the bladder may be intra- or extraperitoneal or combined. The peritoneal surface may be damaged even when the viscus is empty when the missile enters via the perineum and ascends vertically. The intraperitoneal wounds are likely to be complicated by injury to the small intestine, for one or more loops of small gut are usually in contact with the peritoneal surface of the bladder. Very often it is the associated lesion which completely overshadows the bladder injury and not only may it take precedence over the bladder wounds as regards treatment, but the bladder wound is very likely to be overlooked. The pelvic girdle is damaged in about 50% of cases, the rectum is also damaged in about 20% to 30%.

Extraperitoneal injury of the bladder is more common in wartime whereas, in civilian life, intraperitoneal injury is the more common injury.

CLINICAL FEATURES

Shock varies greatly and it is usually due to associated injury or to hæmorrhage. Perforation of the bladder *per se* gives rise to comparatively little shock and an uncomplicated closed rupture, especially if it is intraperitoneal, is notoriously difficult to diagnose in the early stage. Hæmorrhage may be intra- or extravesical. Extravesical hæmorrhage may be intra- or extraperitoneal, depending on the site of the bladder wound. It is frequently difficult to diagnose the type of case that has a concealed hæmorrhage in the form of a large perivesical hæmatoma, tracking retroperitoneally up along the psoas muscles.

Leakage of urine from an external wound is not invariable, because there is a tendency for some bladder wounds to close. The appearance of urine from a buttock wound may be delayed for some hours or even days, especially when there is a long narrow track through the gluteal muscles. Rectovesical wounds give rise to an internal urinary fistula and it is usual for urine to flow into the rectum rather than fæces into the bladder. When any doubt arises as to the nature of a clear effusion from a surface wound, estimation of the urea content should be made. Any figure higher than 0·1% of urea identifies the effusion as urine. Retention of urine after bladder wounds is usual but not invariable, and at the same time urine may be passed without difficulty when the wound is sealed off. Dysuria may occur when a projectile or foreign body is in contact with the bladder neck, though this is not reliable evidence of a retained foreign body. Tenderness and rigidity are unreliable signs and may only indicate a contusion of the abdominal muscle, but these signs must not be confused with those that occur following an intraperitoneal injury when the signs of peritonism are present.

DIAGNOSIS

Various ancillary aids in the diagnosis of bladder injuries have been suggested, such as pneumocystography, cystography using an opaque medium such as sodium iodide, and catheterization of the bladder with the injection and withdrawal of a measured quantity of fluid. These methods are not conclusive or reliable and not always helpful; it is possible to pass the catheter through an intraperitoneal tear in the bladder and withdraw urine from the peritoneal cavity, thus jeopardizing the early diagnosis of a bladder injury.

If a cystogram is required and the time and condition of the patient permit, far more reliable information can be obtained by an intravenous injection of pyelectan. This will show the state of renal function, evidence of any wound of the ureters, whether any foreign body is retained in the bladder, evidence of injuries to the pelvis and lastly evidence of injury to the bladder. If any instrumentation is to be performed, it is far better to perform a cystoscopy. Cystoscopy will give definite evidence of missiles and foreign bodies retained in the bladder and also reveal the sites of wounds, except in gross laceration where it is impossible to fill the bladder to permit of its visualization.

The following routine examination is useful in establishing a diagnosis of bladder injury:

(1) Examine the entrance wound and the wound of exit, if any; a urinary fistula may thus be discovered.

(2) X-ray of the abdomen and pelvis, either straight X-ray in conjunction with an intravenous pyelogram, will locate and show evidence of associated bony damage.

(3) An attempt should be made to reconstruct the pathway of the missile by joining entrance to exit wound or to the site of the retained missile.

(4) Rectal examination should always be undertaken because it will reveal evidence of a perivesical effusion or a rectovesical injury to the pelvic girdle.

The bladder should always be explored in doubtful cases and this was justifiable especially during the war years when through lack of special equipment a full investigation could not be carried out in those patients with a suspected bladder injury. Suprapubic cystostomy with exploration of the perivesical spaces is equivalent to exploratory laparotomy, where the principle of "it is better to look and see rather than to wait and see" applies.

TREATMENT

Each case presents its own peculiar problems and this was very marked in wartime injuries because the majority of these cases were complicated by other injuries and these in themselves were often severe. McAlpine outlined four cardinal principles of treatment as: (1) Excision of the wound in the bladder; (2) suture of the wound; (3) drainage of the bladder; (4) drainage of the pelvic cellular tissue.

Operation should be undertaken at a properly equipped centre at the earliest possible moment to prevent extravasation of blood and urine, to remove any source of infection and to control hæmorrhage.

(1) Formal exploration of the bladder by a suprapubic route. The peritoneum should be opened and the peritoneal surface of the bladder and adjacent pelvic organs carefully inspected and any intraperitoneal lesion should be dealt with then and the rectovesical pouch drained. The bladder should be opened either through a separate incision or by enlarging the existing wound if that is accessible, foreign bodies within the bladder should be removed and all wounds of the wall located and the edges excised.

(2) Perforations are closed by interrupted catgut sutures, including the whole thickness

approached by the suprapubic route, by stripping the bladder from the front of the pubis. An effusion in this space presents in the suprapubic region and may be drained in this region, or it may track along the vas deferens and present in the inguinal region. If there is also damage to the pelvic girdle, the effusion may extend inferiorly along the obturator vessels and nerves deep to the origins of the adductor groups of muscles into the tissues of the thigh and counter-incisions in the inguinal and femoral regions may be needed to provide free drainage.

The posterolateral, or paravesical space, extends behind the bladder in front of the rectum communicating anteriorly with the prevesical space. It is immediately below the rectovesical pouch of the peritoneum and any effusion in it will gravitate between the bladder and the rectum and can be recognized on rectal examination as a diffuse boggy mass above the prostate gland. When the abdomen is opened in such a case, the rectovesical pouch in the male will be found to be diminished in depth by the underlying effusion. The posterolateral or paravesical space is best drained by the perineal route, which route provides dependent drainage.

The fascia in the perivesical spaces has very poor resistance to infection and any effusion into it, whether it be blood or urine, if allowed to remain, will rapidly suppurate. Records of the *1914-18* war showed that pelvic cellulitis was responsible for more deaths than any other single cause in patients who had suffered a bladder wound. It also plays a major part in the morbidity rate following bladder injuries and the late complications such as persistent cystitis, calculus formation, osteomyelitis of the pelvic girdle, infective arthritis of the hip-joint and ascending renal infection, result from a chronic perivesical cellulitis. Osteitis of the symphysis pubis is a common sequel of chronic perivesical cellulitis. Therefore, the most important factor in the treatment of any bladder wound is the prevention of perivesical cellulitis. This is achieved ideally by immediate suture of the wound or wounds of the bladder wall thereby preventing extravasation of urine and blood into the perivesical cellular tissue, and by adequate drainage of this cellular tissue. It is just as important to suture a bladder wound as it is to suture a wound of the gut. At the same time a diversion of the urine by suprapubic cystostomy will put the bladder at rest, prevent leakage of urine through the suture line and allow healing.

The types of injury to the bladder are varied in character and may range from extensive laceration with destruction of large areas of the bladder to contusions of the bladder wall. When the anterior abdominal wall is injured, the bladder may herniate through the wound, giving a condition described by Legueu as "L'extrophie traumatique". Small incisions or puncture wounds of the bladder are often difficult to find on operation, due to the fact that they seal themselves off quite readily but they can be seen on cystoscopy. A common type of wound is a through-and-through wound and a careful search should be made for the exit wound when the missile is not retained in the bladder. The most extensive injuries to the bladder are due to shell or bomb fragments which are low-velocity missiles and readily give rise to infection. Bullet wounds and bayonet stabs are usually clean perforations with little infection. Any missile which strikes the bony pelvis first will cause much soft tissue damage. The pubis, being compact bone, tends to splinter into small fragments when injured by missiles, these splinters being driven into the surrounding tissues ("Blessure à grand fracas", described by Legueu). As the sacrum and ilium are composed largely of cancellous bone, clear-cut perforations or fractures are produced when these are injured and bony fragmentation is far less than when the anterior part of the pelvic girdle is injured.

The track of the missile injuring the bladder is usually an oblique one and it was found by Fullerton that 75% of his cases had wounds in the buttock. Therefore any wound of the buttock should be regarded with suspicion and carefully investigated as soon as possible. Anteroposterior wounds are much less common. Other routes are via the thigh, the groin and the perineum.

Injuries of the bladder may be intra- or extraperitoneal or combined. The peritoneal surface may be damaged even when the viscus is empty when the missile enters via the perineum and ascends vertically. The intraperitoneal wounds are likely to be complicated by injury to the small intestine, for one or more loops of small gut are usually in contact with the peritoneal surface of the bladder. Very often it is the associated lesion which completely overshadows the bladder injury and not only may it take precedence over the bladder wounds as regards treatment, but the bladder wound is very likely to be overlooked. The pelvic girdle is damaged in about 50% of cases, the rectum is also damaged in about 20% to 30%.

Extraperitoneal injury of the bladder is more common in wartime whereas, in civilian life, intraperitoneal injury is the more common injury.

CLINICAL FEATURES

Shock varies greatly and it is usually due to associated injury or to hæmorrhage. Perforation of the bladder *per se* gives rise to comparatively little shock and an uncomplicated

Few cases of true extravasation of urine were seen and they were not of a very serious nature. Three factors probably account for this satisfactory position: (1) Retention of urine follows an injury to the urethra. The patient is unable to micturate. It is usually only when the bladder, if unrelieved, finally overflows that extravasation occurs. (2) A suprapubic cystostomy has usually been carried out long before this critical point is reached. (3) The administration of sulphanilamide drugs and penicillin has helped to keep the tissues sterile.

MISSILE RUPTURES OF THE URETHRA

Fifty-three patients suffering from rupture of the urethra due to penetrating missiles have been treated. The distribution of the lesions is shown in the following table:

55 lesions in 53 patients	Penile urethra ..	14
	Bulbous urethra ..	25
	Posterior urethra ..	16

In two patients double ruptures of the urethra occurred. In the former the bulbous and posterior urethra were separately damaged; in the latter the penile and posterior urethra were injured. The bladder was also injured on three occasions. One patient sustained a double rupture of the urethra and a perforation of the bladder.

The urethra has been wounded by almost every type of missile. It is uncommon to find shell or mortar fragments larger than one inch in length and half an inch in breadth and depth penetrating the pelvis. The larger fragments usually cause such severe injuries that death rapidly supervenes.

Ruptures of the Penile Urethra

Fourteen patients sustained injuries to the penile urethra. The following table shows the types of lesions encountered:

Partial ruptures (8 cases)	Glans penis ..	2	Complete ruptures (6 cases)	Traumatic amputation	2
	Glans and body of penis ..	1		Others	4
	Body of penis ..	5			

In all but three patients the missile traversed the penis in a transverse or slightly oblique direction causing a tangential or through-and-through wound. On two occasions it entered the penis in the region of the glans, passed down the length of the body of the penis injuring the urethra in its course and then travelled on into the perineum or pelvis. In only one instance did a foreign body lodge in the penis.

Partial ruptures.—The partial ruptures of the penile urethra were mainly caused by small missiles. With one exception all had a suprapubic cystostomy performed to divert the urine from the urethra.

Two of the three cases of injury to the glans and adjacent body of the penis required plastic repairs. One healed completely ; in the other a minute urinary fistula persisted on the under-surface of the penis.

Of the five patients suffering from wounds of the shaft of the penis it had been found impossible to catheterize two at Forward Units. With careful manipulation, however, it was later found possible to pass a catheter and the partial continuity of the urethra was thus proven. One of the earliest of these patients was treated with an indwelling catheter as a splint. This treatment was, however, later abandoned and once continuity of the urethra had been demonstrated no catheter was left in position and no further treatment was given except the occasional passage of a sound. In no case was the urethra sutured. Secondary suture of the skin wounds was carried out in three patients.

Complete ruptures.—In two patients traumatic amputation of the penis had occurred. In each instance the penis had been cut across about one inch distal to the pubis and the skin torn away from the remaining stump up to the level of the pubis. Both cases were complicated by severe adjoining wounds of the left groin and in one the posterior urethra and bladder were also injured. It was evident in each case that if the remaining stump was not covered with skin gross fibrosis and retraction would occur and render the organ practically useless. In both patients the adjoining injuries rendered immediate grafting impossible and it was several weeks before they were fit for treatment. By this time considerable retraction had occurred and the stump of the penis in each instance required mobilization from a bed of granulation tissue. The stump of the penis was then covered by a pedicle skin flap cut from the scrotum. One case was completely successful and before returning to the United Kingdom was able to use his penis to micturate through the fly of the trousers. This patient has since informed me that he has full control of micturition. In addition erections of the penile stump occur and intercourse is possible. In the second patient the scrotal flap was cut a little too narrow at its base and some terminal necrosis occurred. He, however, of the wall. It is often seen that small punctures or incised wounds of the bladder, particularly those affecting the peritoneal surface, may have a tendency to come together and seal themselves off. Too much reliance should not be placed on this as a safeguard against subsequent leakage of urine and it is better to suture a wound however small it may be.

(3) Suprapubic drainage of the bladder should always be undertaken however small the perforation or wound may be. This method of drainage, though it has many critics, does put the bladder at rest and by diverting the flow of urine prevents leakage through the suture line.

An indwelling urethral catheter, except as an emergency method of treatment to get a patient to hospital at a distance, has no place in the treatment of bladder wounds, however slight they may be. Drainage is uncertain, and it is not possible to drain a bladder *per urethram* for a sufficient length of time to allow the bladder to heal and to correct any urinary infection, also the small eye of the catheter is very likely to become blocked with mucus or blood clot converting the catheter into a plug instead of a drain.

There appears to be great reluctance on the part of some general surgeons to do a suprapubic cystostomy in order to drain the bladder with the mistaken belief that a persistent suprapubic fistula is likely to result. If a persistent fistula occurs, it is due to infection resulting either from an overlooked foreign body in the bladder or from a perivesical cellulitis. In the absence of infection and obstruction to the normal passage of urine, a suprapubic sinus will always close quite rapidly after the tube has been removed.

(4) Careful exploration of perivesical tissues adjacent to any extraperitoneal wound of the bladder should be carried out. The extravesical hæmorrhage is controlled and any foreign body removed. Free drainage of the perivesical tissues adjacent to the bladder wound is most essential and in this respect it may be necessary to use counter-incisions in the groins, medial aspect of the thigh or the perineum where perivesical cellulitis is widespread.

Before laparotomy, wounds of the buttock should be explored from behind, a tube should be inserted into the depths of the wound to drain the pelvic cellular tissues, as adequate drainage from the abdomen is often impossible. Associated wounds of the rectum should be treated by diversion of the flow of fæces by a left iliac or transverse colostomy. An attempt should be made to suture the rectal wall and drain the perirectal tissue. This often involves removal of the coccyx or often part of the sacrum as was suggested by Sir Charles Gordon-Watson. Any associated injury of the lower end of the ureter should be treated by reimplantation into the bladder in such a position that the site of anastomosis is free from tension.

Injuries of the Urethra [*Abridged*][1]

By D. S. Poole-Wilson, F.R.C.S.

In outlining a policy for the treatment of urethral injuries by Forward Units in the Field it had to be recognized that operative facilities were sometimes not too good, that the patient's general condition frequently did not warrant a prolonged operation and that the after-care might not be entirely satisfactory. Under these circumstances surgeons were advised to avoid carrying out complicated urethral repairs and to be content with performing a toilet of the wounds, a suprapubic cystostomy to relieve retention and divert the urine from the injured area, and when necessary incision and drainage to relieve extravasation or very large hæmatomata.

Following this primary treatment patients were, whenever possible, evacuated back to the G.U. Centre for definitive treatment. It is thus evident that the work which I am submitting in this communication has been contributed to by almost every surgeon serving in a Forward Unit in the Central Mediterranean Force.

A total of 81 patients suffering from ruptures of the urethra were observed. 53 of these patients had missile injuries of the urethra; the remaining 28 were accidental ruptures.

In the majority of patients primary surgical operations had been carried out at Field Surgical Units or Casualty Clearing Stations and the patients reached the G.U. Centre at varying periods from twenty-four hours after injury. The standard of diagnosis was high and in the vast majority of patients the urethral lesion had been noticed shortly after wounding or injury. Suprapubic cystostomy was almost invariably used to divert the urine from the urethra. These patients travelled extremely well. In a few instances perurethral catheter drainage was used but all subsequently required a suprapubic cystotomy. These patients travelled badly as the urethral catheters usually became either blocked or lost in transit. Relatively few attempts were made at the primary operation to repair the urethra. When the posterior urethra was damaged, however, an indwelling catheter was frequently fixed in position to act as a splint and prevent any loss of urethral alignment.

---

[1] The material used in this Paper regarding missile injuries of the urethra is condensed from a Hunterian Lecture on Missile Injuries of the Urethra delivered in 1946 and which it is hoped will be published shortly.

Few cases of true extravasation of urine were seen and they were not of a very serious nature. Three factors probably account for this satisfactory position: (1) Retention of urine follows an injury to the urethra. The patient is unable to micturate. It is usually only when the bladder, if unrelieved, finally overflows that extravasation occurs. (2) A suprapubic cystostomy has usually been carried out long before this critical point is reached. (3) The administration of sulphanilamide drugs and penicillin has helped to keep the tissues sterile.

MISSILE RUPTURES OF THE URETHRA

Fifty-three patients suffering from rupture of the urethra due to penetrating missiles have been treated. The distribution of the lesions is shown in the following table:

55 lesions in 53 patients	Penile urethra ..	14
	Bulbous urethra ..	25
	Posterior urethra ..	16

In two patients double ruptures of the urethra occurred. In the former the bulbous and posterior urethra were separately damaged; in the latter the penile and posterior urethra were injured. The bladder was also injured on three occasions. One patient sustained a double rupture of the urethra and a perforation of the bladder.

The urethra has been wounded by almost every type of missile. It is uncommon to find shell or mortar fragments larger than one inch in length and half an inch in breadth and depth penetrating the pelvis. The larger fragments usually cause such severe injuries that death rapidly supervenes.

Ruptures of the Penile Urethra

Fourteen patients sustained injuries to the penile urethra. The following table shows the types of lesions encountered:

Partial ruptures (8 cases)	Glans penis ..	2	Complete ruptures (6 cases)	Traumatic amputation	2
	Glans and body of penis ..	1		Others	4
	Body of penis ..	5			

In all but three patients the missile traversed the penis in a transverse or slightly oblique direction causing a tangential or through-and-through wound. On two occasions it entered the penis in the region of the glans, passed down the length of the body of the penis injuring the urethra in its course and then travelled on into the perineum or pelvis. In only one instance did a foreign body lodge in the penis.

Partial ruptures.—The partial ruptures of the penile urethra were mainly caused by small missiles. With one exception all had a suprapubic cystostomy performed to divert the urine from the urethra.

Two of the three cases of injury to the glans and adjacent body of the penis required plastic repairs. One healed completely; in the other a minute urinary fistula persisted on the under-surface of the penis.

Of the five patients suffering from wounds of the shaft of the penis it had been found impossible to catheterize two at Forward Units. With careful manipulation, however, it was later found possible to pass a catheter and the partial continuity of the urethra was thus proven. One of the earliest of these patients was treated with an indwelling catheter as a splint. This treatment was, however, later abandoned and once continuity of the urethra had been demonstrated no catheter was left in position and no further treatment was given except the occasional passage of a sound. In no case was the urethra sutured. Secondary suture of the skin wounds was carried out in three patients.

Complete ruptures.—In two patients traumatic amputation of the penis had occurred. In each instance the penis had been cut across about one inch distal to the pubis and the skin torn away from the remaining stump up to the level of the pubis. Both cases were complicated by severe adjoining wounds of the left groin and in one the posterior urethra and bladder were also injured. It was evident in each case that if the remaining stump was not covered with skin gross fibrosis and retraction would occur and render the organ practically useless. In both patients the adjoining injuries rendered immediate grafting impossible and it was several weeks before they were fit for treatment. By this time considerable retraction had occurred and the stump of the penis in each instance required mobilization from a bed of granulation tissue. The stump of the penis was then covered by a pedicle skin flap cut from the scrotum. One case was completely successful and before returning to the United Kingdom was able to use his penis to micturate through the fly of the trousers. This patient has since informed me that he has full control of micturition. In addition erections of the penile stump occur and intercourse is possible. In the second patient the scrotal flap was cut a little too narrow at its base and some terminal necrosis occurred. He, however, now has full control of micturition from the stump. Erections occur but owing to the severe injuries in the left groin the penile stump becomes drawn over to the left side.

Two of the remaining four cases of complete rupture of the penile urethra were complicated by gross penile damage. In one patient it was possible to pass a finger completely through the penis. At the Field Surgical Unit it was felt that the distal portion would inevitably become gangrenous but it was wisely decided to leave it attached. This soldier was seen on the fourth day after injury. His wound was clean. The ends of the urethra were found and mobilized and a complete suture performed around a catheter arranged for penicillin irrigation. The corpora cavernosa penis were repaired as far as possible and the subcutaneous tissue and skin sutured. Complete healing, except for a minute sinus leaking about five drops of urine per act of micturition, was obtained. The other case of complete rupture was also treated by suture of the urethra and delayed primary suture of the cutaneous wounds with complete success.

The two remaining instances of complete rupture were fairly old injuries in two Jugo-Slav Partisans. One patient, a boy of 15 years, had sustained a wound of the penis resulting in complete occlusion of the urethra. He had been draining by the suprapubic route for over a year. Complete excision of the fibrous occluded section was carried out and full normal micturition restored. The second Jugo-Slav patient had also sustained a through-and-through wound of the penis, which had resulted in occlusion of the urethra. Attempts had been made to restore continuity but had resulted in a peno-scrotal fistula. It was evident that to close the fistula and restore continuity a large block of fibrous tissue would have to be excised and the cut ends of the urethra united. The operation was difficult but proved successful.

Ruptures of the Bulbous Urethra

Twenty-five patients suffering from rupture of the bulbous urethra have been treated and are classified as follows: Contusion urethra 3; partial rupture 16; complete rupture 6.

Contusion of the urethra was diagnosed when, following a wound in the region of the urethra, retention or urethral bleeding occurred but no difficulty was experienced in passing a catheter and no perforation of the urethra was demonstrated in the adjacent wound. In two of the three cases there were extensive groin and perineal wounds, which required extensive plastic repairs.

Partial ruptures.—Sixteen partial ruptures of the urethra were treated and were mainly caused by projectiles passing anteroposteriorly across the perineum. A few were due to mine and shell wounds, which entered the perineum from below. Apart from the passage of a catheter to demonstrate the continuity of the urethra eleven patients required no operative treatment on the urethra. Removal of foreign bodies and delayed primary suture of perineal wounds were, however, carried out. In five instances repairs of the urethra were performed. It is noteworthy that in eight of these sixteen partial ruptures it had been found impossible to pass a catheter at the original operation carried out at a Forward Unit and that in five of these patients no further urethral operation was eventually found necessary.

Complete ruptures.—Six cases of complete rupture of the bulbous urethra have been treated. One patient, who was suffering from multiple injuries and a complete occlusion of the urethra, died from infective jaundice before any repair was attempted. Of the remaining five two had undergone unsuccessful repairs before admission to the Centre and required further operative treatment; the other three had complete repairs of the urethra carried out. It has always been possible to mobilize the ends of the urethra after the manner of Marion sufficiently to bring them together and to obtain complete suture over a catheter, which has then been withdrawn. The technique of bridging a gap with an indwelling catheter, or suturing the roof and leaving the perineal wound to granulate over, has never been resorted to. The perineal wounds have all been closed but a penicillin irrigation tube has frequently been left in position. Young's technique of closing large flaps in the bulbous urethra by liberating the attachments of the penis within the scrotum and drawing the corpora cavernosa and spongiosum backwards has never been employed. It is, however, noteworthy that Young claims that gaps of even four inches can be closed by this means. Likewise the method of Pasteur and Iselin has not been used.

The use of penicillin, both intramuscularly and by local and urethral irrigation, allowed closure of perineal wounds, which would otherwise have been left to granulate. Healing has thus been accelerated and there can be little doubt that the resulting decrease in scar tissue meant less tendency to stricture formation.

Ruptures of the Prostato-Membranous Urethra

Sixteen missile ruptures of the posterior urethra have been treated. The injury may involve any portion of the posterior urethra.

A catheter can seldom be passed in these patients and it is therefore impossible to divide them satisfactorily into partial and complete ruptures. There is, however, little doubt that in many the continuity of the urethra is not completely broken. The wounds of the membranous urethra seem to be the most dangerous from the point of view of stricture formation. Complete ruptures at the junction of the prostatic and membranous urethra with posterior dislocation of the prostate on the urogenital diaphragm, such as occur in severe traumatic fractures of the pelvis in civil life, were not seen.

The rectum has been injured on six occasions but only two prostato-rectal fistulæ have failed to close spontaneously and have required separation and closure.

The danger of stricture formation in the region of the membranous urethra, and the great difficulty of treating this condition satisfactorily at a later date, have led me invariably to use an indwelling urethral catheter as a splint. It is probable that this is unnecessary in many wounds involving the bladder-neck or body of the prostate, and that the rigidity of the remaining prostatic wall is sufficient to prevent the ends of the urethra getting out of alignment. Nevertheless the difficulty of estimating the exact extent of the wound and the seriousness of an unsuccessful outcome seem to make an indwelling catheter imperative.

Two methods have been used to introduce the indwelling catheter: (1) In the first method a finger is passed down into the posterior urethra and it is then frequently possible to guide the tip of a Lister's sound, which has been passed down the anterior urethra, into the bladder. The distal end of a small rubber catheter is then slipped over the tip of the sound so that it grips firmly and the catheter is drawn through the urethra by withdrawing the sound.

(2) In the more difficult cases, where the rupture is in the region of the membranous urethra, two Lister's sounds are used, the tip of one of which has been slightly hollowed out so as to form a cup in which the tip of the other may engage. The female sound is passed through the internal urethral orifice and the plain one down the anterior urethra. The two sounds are gently manipulated until the points engage. These are then held firmly together, whilst the distal sound is carried forwards into the bladder. The distal end of a rubber catheter is then slipped over its tip and drawn back down the urethra. These two methods have always been successful and no perineal explorations have been necessary. In addition the operation can frequently be carried out by slipping a finger down the suprapubic track and it is seldom necessary to reopen the suprapubic wound entirely.

The indwelling catheter is held in position by a stitch through its tip, which is brought out alongside the suprapubic Malecot catheter and tied to a piece of rubber tubing on the abdominal wall. This technique also ensures that subsequent catheters can, if necessary, be drawn through the urethra. The catheter is not really for use as a drain but as a urethral splint. Prior to introduction a piece of thread is tied around the catheter immediately distal to the eye. This prevents drainage down the catheter and allows of one tube the less to be attached to a bottle. If the catheter is not draining, it is also easier to keep the catheter and urethra sterile as the whole of the perineum and penis can be covered over with sterile dressings. This catheter is also frequently used for penicillin irrigation of the urethra by cutting an eye distal to the ligature mentioned above (*see* fig. 1).

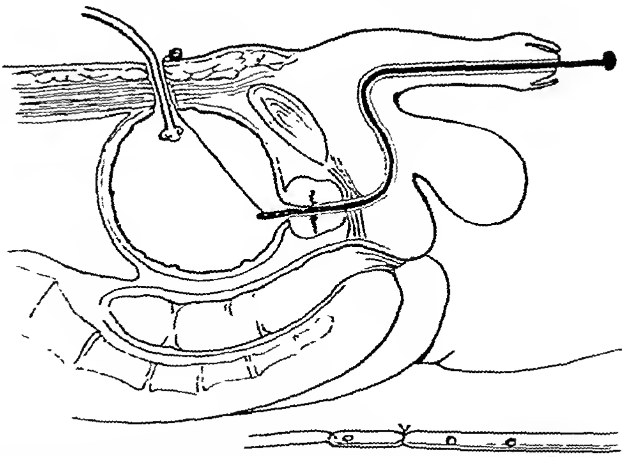


FIG. 1.—Illustrating method of fixing a urethral catheter as a urethral splint. The inset shows a catheter arranged for penicillin irrigation.

The urethral catheter is left in position for at least two weeks so as to ensure firm fixation of the ends of the urethra.

In two patients prostato-rectal fistulæ required operation. An inverted V perineal incision was made and separation of the rectum and prostate carried out to a level well above that of the fistula. The fistula in the posterior margin of the prostate was then sutured and the rectal opening invaginated and oversewn with two layers of sutures. The perineum was closed with a small penicillin irrigation tube in position.

ACCIDENTAL RUPTURES OF THE URETHRA

Twenty-eight cases of accidental rupture of the urethra came into the Genito-Urinary Centre. These were divided as follows:

Rupture of bulbous urethra	8	*Rupture of posterior urethra*	20
Contusion	1	Complete	9
Partial rupture ..	7	Partial	11
Complete rupture ..	0		

Ruptures of the Bulbous Urethra

With one exception all the ruptures of the bulbous urethra resulted from various types of blows in the perineum. The exception was a patient in whom a Tobruk plaster had been applied too tightly. An area in the perineum about two and a half inches in diameter became necrotic and finally sloughed away leaving the two open ends of the urethra exposed in a bed of granulation tissue and joined by a thin strand of the roof of the urethra.

At the primary operation one patient appeared to have sustained little more than a contusion of the urethra. He was catheterized with ease and as the urethral bleeding had been slight and as no perineal hæmatoma was present no further operative treatment was carried out. He had a little trouble in starting micturition and then passed urine very satisfactorily.

The patient suffering from the necrosis of the perineum had a suprapubic cystostomy performed to divert his urine. At a later date a very extensive plastic repair was carried out and the ends of the urethra were mobilized, brought together and sutured. The scrotum was brought back to cover the perineum. Complete healing occurred and normal micturition was restored.

Of the remaining six cases catheterization failed at the primary operation in five instances. These ruptures were all eventually shown to be partial and the failure to pass a catheter was probably due to the lack of rubber coudé catheters with Forward Units. The primary operations carried out on these patients varied. Two patients had a suprapubic cystostomy alone performed. Both of these patients had a perineal exploration of the urethra carried out a few days later. The rupture in each case was found to be partial and was sutured over an indwelling catheter. The perineum was closed except for a small drain. Both of these patients made extremely good recoveries.

Another patient had a suprapubic cystostomy and a perineal incision to evacuate a hæmatoma. On examining him a few days later a coudé catheter ran easily into the bladder. The perineal wound was clean, and on inspection a partial tear was seen in the urethra. This was sutured. No indwelling catheter was left in position. The perineum was sutured with drainage. Complete and rapid healing occurred.

A further patient had a suprapubic cystostomy, and as attempted catheterization had failed the two-sound method was used and an indwelling urethral catheter eventually drawn back into position. This patient made a very satisfactory recovery.

The remaining two patients had suprapubic cystostomy and perineal exploration carried out at their primary operations under difficult circumstances. Both had incomplete ruptures and in each an indwelling catheter was placed in position and the perineal wound left open. Both of these patients ran an unsatisfactory course. The first developed a perineal sinus, which only closed after two further operations. He was finally evacuated home, but his perineum again broke down. Closure finally occurred but a left pyonephrosis necessitated removal of the left kidney. The second patient developed an abscess in his left groin and a mild osteitis of the pubis. Healing finally occurred.

Traumatic Rupture of the Posterior Urethra

Twenty cases of accidental rupture of the posterior urethra have been seen. With one exception, where the cause is unknown, they were the result of traffic accidents. The pelvis was fractured in all but one instance and the fractures were severe in type. In the single instance where the pelvis was not fractured a partial rupture of the prostato-membranous urethra was caused by the kick starter of a motor-cycle passing through the anus and perineum into the prostate.

At the primary operation it was found possible to divide these patients into cases of complete and incomplete rupture. In the literature much confusion exists regarding the site of the ruptures. Some authors describe the majority of them as involving the membranous urethra; others deny having ever seen a rupture of the membranous urethra. Observation is difficult as the floor of the pelvis is always covered with much blood clot. In the present series, however, the complete ruptures appeared to result from the bladder with the prostate attached being sheared off the upper surface of the pelvic diaphragm. The partial ruptures appeared to be due to a deficiency in the anterior wall of the junction of the prostatic and membranous urethra. It was not always possible to decide whether this resulted from a splitting of the pelvic diaphragm with a tear running back into the urethra, avulsion of part of the lower anterior wall of the prostatic urethra or a shearing of the prostate off the pelvic diaphragm, which has just failed to become complete.

Complete rupture of the posterior urethra.—Nine cases of complete rupture were treated. In every one the bladder with the prostate attached was torn off the upper surface of the pelvic diaphragm and displaced backwards. Despite the severity of the injury extravasation of the urine was not always present and in at least three instances the bladder was found distended with urine and yet there was none in the pelvic tissues. The internal sphincter appeared to be quite capable of retaining the urine in the bladder.

At the primary operation a suprapubic cystostomy was performed in all cases and in seven an indwelling urethral catheter was drawn down the urethra. In the remaining two patients the suprapubic wound was opened a few days later and a urethral splint drawn into position. Primary repair by the perineal route as advocated by Hugh Young was never performed.

In two patients alignment of the urethra was lost following removal of the indwelling catheter. In one patient continuity was restored by reopening the suprapubic wound slightly and using the two-sound method. In the other the perineum had to be explored through an inverted V incision and the continuity of the prostatic and membranous urethra restored.

Partial rupture.—Eleven cases of partial rupture of the posterior urethra have been seen. Two of these were complicated by separate extraperitoneal ruptures of the bladder.

At the primary operation six of these patients had a suprapubic cystostomy and an indwelling urethral catheter drawn into position. Two of these patients also had an extraperitoneal rupture of the bladder closed.

Three patients had only a suprapubic cystostomy performed at their primary operation. On subsequent examination it was possible to pass a catheter on two of them. The third patient had to have his suprapubic wound reopened and an indwelling catheter drawn through by the double-sound method.

The patient whose perineum had been injured by the kick starter of his motor-cycle had a suprapubic cystotomy and exploration of his perineum performed at his primary operation. A prostato-rectal fistula persisted. This was later explored by the perineal route and the openings in the prostate and rectum closed.

One patient who was catheterized with ease at his primary operation was thought to have little more than a urethral contusion. The catheter was removed and he passed urine freely for a day. He then developed retention, which was relieved by an indwelling catheter. This patient had a very severe dislocation of the symphysis pubis, with a fracture of the right pubic arch and a dislocation of the right sacro-iliac joint. Attempts were made to reduce this dislocation by manipulation but were not very successful. On the eighth day his catheter was removed. On attempting to pass urine, a trickling sensation was felt in the right groin and an extravasation of urine occurred. A suprapubic cystostomy was immediately performed. A catheter still ran easily into the bladder showing that the rupture was incomplete. It seems probable that the manipulation of the pelvis or its instability had either increased the rupture or prevented its peritoneal healing. Two other patients, who had unstable pelves, also lost the continuity of the urethra during convalescence either by increase in the severity of the rupture or possibly due to stricture formation. Continuity was restored by the double-sound method in one and by open exploration of the perineum in the other. It thus became very evident that if the pelvic girdle is unstable and cannot be controlled the indwelling catheter must be retained for a longer period than usual.

The following table shows the results obtained:

(1) Returned to duty (Category B 1)	18
(2) Invalided home. Passing urine normally	46
(3) Invalided home. Passing urine normally apart from a minute urethral fistula	3
(4) Invalided home with suprapubic drainage. Urethral channel present in all	12
(5) Death	2

The urethral catheter is left in position for at least two weeks so as to ensure firm fixation of the ends of the urethra.

In two patients prostato-rectal fistulæ required operation. An inverted V perineal incision was made and separation of the rectum and prostate carried out to a level well above that of the fistula. The fistula in the posterior margin of the prostate was then sutured and the rectal opening invaginated and oversewn with two layers of sutures. The perineum was closed with a small penicillin irrigation tube in position.

ACCIDENTAL RUPTURES OF THE URETHRA

Twenty-eight cases of accidental rupture of the urethra came into the Genito-Urinary Centre. These were divided as follows:

Rupture of bulbous urethra	8	*Rupture of posterior urethra*	20
Contusion	1	Complete	9
Partial rupture ..	7	Partial	11
Complete rupture ..	0		

Ruptures of the Bulbous Urethra

With one exception all the ruptures of the bulbous urethra resulted from various types of blows in the perineum. The exception was a patient in whom a Tobruk plaster had been applied too tightly. An area in the perineum about two and a half inches in diameter became necrotic and finally sloughed away leaving the two open ends of the urethra exposed in a bed of granulation tissue and joined by a thin strand of the roof of the urethra.

At the primary operation one patient appeared to have sustained little more than a contusion of the urethra. He was catheterized with ease and as the urethral bleeding had been slight and as no perineal hæmatoma was present no further operative treatment was carried out. He had a little trouble in starting micturition and then passed urine very satisfactorily.

The patient suffering from the necrosis of the perineum had a suprapubic cystostomy performed to divert his urine. At a later date a very extensive plastic repair was carried out and the ends of the urethra were mobilized, brought together and sutured. The scrotum was brought back to cover the perineum. Complete healing occurred and normal micturition was restored.

Of the remaining six cases catheterization failed at the primary operation in five instances. These ruptures were all eventually shown to be partial and the failure to pass a catheter was probably due to the lack of rubber coudé catheters with Forward Units. The primary operations carried out on these patients varied. Two patients had a suprapubic cystostomy alone performed. Both of these patients had a perineal exploration of the urethra carried out a few days later. The rupture in each case was found to be partial and was sutured over an indwelling catheter. The perineum was closed except for a small drain. Both of these patients made extremely good recoveries.

Another patient had a suprapubic cystostomy and a perineal incision to evacuate a hæmatoma. On examining him a few days later a coudé catheter ran easily into the bladder. The perineal wound was clean, and on inspection a partial tear was seen in the urethra. This was sutured. No indwelling catheter was left in position. The perineum was sutured with drainage. Complete and rapid healing occurred.

A further patient had a suprapubic cystostomy, and as attempted catheterization had failed the two-sound method was used and an indwelling urethral catheter eventually drawn back into position. This patient made a very satisfactory recovery.

The remaining two patients had suprapubic cystostomy and perineal exploration carried out at their primary operations under difficult circumstances. Both had incomplete ruptures and in each an indwelling catheter was placed in position and the perineal wound left open. Both of these patients ran an unsatisfactory course. The first developed a perineal sinus, which only closed after two further operations. He was finally evacuated home, but his perineum again broke down. Closure finally occurred but a left pyonephrosis necessitated removal of the left kidney. The second patient developed an abscess in his left groin and a mild osteitis of the pubis. Healing finally occurred.

Traumatic Rupture of the Posterior Urethra

Twenty cases of accidental rupture of the posterior urethra have been seen. With one exception, where the cause is unknown, they were the result of traffic accidents. The pelvis was fractured in all but one instance and the fractures were severe in type. In the single instance where the pelvis was not fractured a partial rupture of the prostato-membranous urethra was caused by the kick starter of a motor-cycle passing through the anus and perineum into the prostate.

In these latter cases, while the kidney may often be grossly disrupted, the investing renal fascial planes are intact, with the result that, not only may the hæmorrhage be at least temporarily limited in extent, but also the increasing rise in subfascial tension gives rise to increasing pain.

In penetrating injuries, on the other hand, the fascia of Zuckerkandl, and the true renal fascia and sometimes also the peritoneum, are also torn and disrupted, and blood can escape in almost all directions, and so local tension does not rise, and pain does not increase nor a tumour appear. The pulse-rate is, in fact, the only safe guide to continued bleeding.

For the repair of the renal parenchyma, No. I non-chromic catgut threaded on a blunt-pointed Kouznetzoff needle, curved on the flat, was used. Interrupted ordinary sutures are preferred to mattress sutures, as there is slightly less chance of producing a further ischæmia of the already damaged renal tissue. The hæmostatic value of these stitches, tied as loosely as one dare, can be further increased by applying strips of muscle cut from the parietes, to the renal tear or tears, before tying the knots.

No attempt should be made to close a hole in the pelvis, though it should be partially sutured if it is a big tear, and it can also be used for the pyelotomy, which is, of course, essential.

The damaged renal pedicle is, in some respects, a unique problem in its urgency, in that the pressure in the renal artery, arising straight from the aorta near to the heart is high, even in shocked subjects, while the venous pressure is negative or near negative. At the moment of operation therefore, when the area is opened up, the increase in bleeding may be considerable, and the chances of an air embolism are also increased if the vein is torn.

It is this urgency which may sometimes stampede a surgeon into doing a quick nephrectomy without giving himself time to investigate the exact extent of the damage.

This urgency can be satisfied, and sometimes the kidney preserved, if, at the moment the kidney is exposed, the renal pedicle, together with its surrounding fat and blood-infiltrated tissue, be lightly but effectively grasped in a pair of sponge forceps, or a rubber-covered duodenal clamp. This will give time, while the bleeding is controlled, to make a more deliberate dissection of the pedicle, to see just what has happened.

It will often then be found that only a portion of the vascular pedicle is damaged, in or near the renal parenchyma, and that a ligature applied to damaged sub-branches of the main vessels may still leave an organ which is worth preserving.

One case was a paratrooper admitted six hours after wounding, with a large wound of entry only, in the left subcostal region, and hæmaturia. Except around the kidney, there was no muscle guarding, the pulse was rising steadily, and there was no audible peristalsis. This latter was due to the grain of morphia that he had geen given at the battalion H.Q.

At operation a large shell fragment was found and removed from the kidney substance and at the end of the operation the peritoneum was opened as a precaution and was found to contain blood. A second incision was therefore made and the peritoneum widely explored, when it was found that there was in fact no intraperitoneal injury, but that about half a pint of blood had entered the abdomen from a peritoneal tear on the anterior surface of the damaged kidney. I feel that this second incision and inevitable lengthening of the operation could have been avoided had the kidney been approached originally through a paramedian incision.

In one case only was a left kidney removed through a transdiaphragmatic approach. This man had a wound of entry in the left arm; the bullet had crossed into his left chest and he had hæmaturia and no wound of exit. The man was in great distress from a sucking pneumothorax. A large tear was found in the diaphragm, and by enlarging this still further a totally disrupted left kidney was removed without difficulty. As the metal fragment had not been found the peritoneum was also opened and an exploration satisfied me that the fragment had not left the perirenal fat, and the search was discontinued. The patient made a good recovery.

The late results of ureteral anastomosis are not impressive and in battle casualties there is the further complication of sepsis round the ureterocutaneous fistula, and a portion of the ureter may even be shot away, making anastomosis without tension impossible.

For section of the lower ureter, reimplantation into the bladder gives good results, or, if this cannot be done without tension, then a flap of bladder can be turned up, and fashioned into a sleeve, and joined to the cut end of the ureter.

For the upper lengths of the ureter, the little operation of transplantation into the extraperitoneal, or extraperitonealized colon, is well worth trying, before resorting to nephrectomy.

Mr. Parker recorded fourteen cases of bladder injury, all except one being associated with other visceral damage. In one case, the shell fragment was actually in the bladder lumen.

General Observations on Treatment

In ideal surroundings and with a patient in good condition it is often quite possible and reasonable to carry out suprapubic drainage of the bladder and a complete repair of the urethra at the primary operation. When these conditions do not exist suprapubic drainage to divert the urine together with a toilet of any perineal wounds as a primary operation and a subsequent secondary repair have given excellent results. In fact it is probable that at times these results may be superior to those obtained by a complete primary operation. In cases of complete rupture of the posterior urethra, however, alignment should be restored and maintained by an indwelling catheter at as early a time as possible.

The principles of delayed primary suture hold for perineal wounds involving the urethra. It is most desirable to avoid large granulating wounds in the perineum as they render the tissues rigid and in the event of a urethral repair being unsatisfactory make subsequent operations extremely difficult. Using parenteral and irrigation penicillin almost all perineal wounds have been completely closed.

A considerable apprenticeship is necessary to learn the art of urethral repair. The importance of an unhurried operation, good exposure, a bloodless field, adequate mobilization of the urethra and suture without tension must be stressed. Fine instruments are essential. Plain 6/0 catgut is used for the urethral suture.

Indwelling catheters should be used as little as possible. The presence of a foreign body in the urethra retards healing. For splinting the posterior urethra a small size is used (15 F.) so as to allow free drainage down the urethra around it.

Penicillin has been used very extensively both intramuscularly and for the irrigation of the urethra and perineal wounds.

In no form of surgery is good after-treatment more important. Suprapubic tubes must be kept draining perfectly. Very large perineal dressings must be used to keep the wounds aseptic.

No definite time can be laid down for the healing of urethral wounds. Suprapubic drainage should be continued until all perineal and urethral wounds are healed. No urine should pass down the urethra until this time is reached. When the time is due to try the restoration of normal micturition a spigot is placed in the suprapubic tube and the patient encouraged to pass urine through his urethra. If any leakage from perineal or penile wounds occurs the suprapubic drainage must be continued; but if after a few days all wounds remain absolutely dry then the suprapubic catheter is removed and the wound allowed to heal. Leakage from the healing suprapubic wound is slight as the patient has already learnt to micturate. Indwelling catheters should not be used to aid the closure of the suprapubic wound as it is unwise to risk starting even the mildest urethritis.

Some Observations on a Personal Series of Battle Casualties Involving the Genito-Urinary System. [*Abridged*]

By Geoffrey E. Parker, F.R.C.S.

In a series of 94 abdominal operations done in the forward areas of Africa and Italy, no less than 36 involved, among other things, the urinary apparatus.

There were 17 kidney injuries—in one case bilateral—14 bladder injuries and 5 cases with wounds of the prostate and prostatic urethra.

The overall recovery rate was 67% but as the great majority of the cases had injuries involving much more than the genito-urinary system, these specific injuries alone could not be blamed for the mortality of 33%.

Of the 17 renal cases which came to operation it was found possible to preserve and repair the kidney in 8. All the 8 cases treated conservatively involved injury to the parenchyma and, in 4 of them, the renal pelvis was also torn open.

There is no doubt that the proportion of cases in which the kidney could have been preserved would have been higher still but for the fact that so many other lesions, such as bleeding mesenteric vessels, torn and perforated bowel and liver, had also to be dealt with, and quickly; and so it often seemed more expedient to take out the damaged kidney, after confirming the presence and integrity of the other one, in order quickly to deal with no less urgent problems elsewhere in the abdomen.

In the absence of signs and symptoms of other visceral injury, the decision to operate was determined by a number of factors; the rise in pulse-rate, the spread of rigidity on the affected side, the increasing pain, and lastly and of less importance an increasing tumour in the loin.

With regard to physical signs of renal injury, the significance of pain and tumour differs in battle casualties from the crushing type of injury more often seen in civil practice.

I can recall a kidney injury from a large flying bomb fragment very similar to Mr. Parker's case. It entered through the left eleventh rib in the mid-axillary line, ploughed through the lower lobe of the lung, the diaphragm, and remained embedded in the left kidney. The missile laid open an approach which after wound excision and extension strongly resembled the Bernard Fey approach to the kidney, a method I frequently use for exploration of the kidney and suprarenal. In this case excellent opportunity was offered for closure of a hole in the pericardium, a large tear in the diaphragm and pleura, and left nephrectomy. Except for development of a fæcal fistula on the tenth day from bruising of the splenic flexure, which quickly closed spontaneously, and delayed recovery of the lung injury, convalescence was satisfactory. The patient, a senior officer, was able to return to duty four months after injury.

Finally, as to the emplacement of the splint catheter for ruptures of the prostato-membranous urethra with broken alignment, many ingenious methods are described. May I point out one I cannot remember having seen recorded and which has the virtue of simplicity, namely reduction of the prostate forwards by a finger in the rectum. On two occasions (on the ninth and fourteenth days after injury respectively) mere suprapubic drainage had been established when the cases reached me. Passing a Lister bougie with my left hand and with my right index finger in the rectum I pushed the prostate forward and so was able to direct the bougie across the rupture up through the prostatic urethra. My assistant meanwhile had his finger in the bladder through the drainage opening and so was able to tell me when the bougie entered through the internal urinary meatus. A rubber tube was then stretched over the bougie's point and so withdrawn through the urethra as described by Mr. Poole-Wilson.

Thus every variety of urogenital injury was witnessed on the home front including my three cases of gun-shot wounds of the ureter which were reported in the *British Journal of Urology*, 1946, 18, 166.

Mr. Mogg, in reply, stated that while he agreed with the majority of Mr. Everidge's views and appreciated his sound judgment and wealth of experience in traumatic urological surgery, he still thought it advisable to attempt to close wounds of the lateral walls of the bladder. This, in conjunction with suprapubic cystostomy, did prevent extravasation of urine into the pelvic cellular tissue and prevent pelvic cellulitis with all its unfortunate sequelæ.

[*April* 24, 1947]

Treatment of Hydronephrosis Associated with Abnormal Vessels[1]

By H. HAMILTON STEWART, F.R.C.S.

SOME surgeons hold the view that the mechanical obstruction caused by a lower polar or aberrant artery is a secondary obstruction. They consider that the primary enlargement of the renal pelvis is caused by a neuromuscular defect, or a congenital stricture, and that if a lower polar or aberrant artery is present, then a superimposed mechanical obstruction occurs.

I do not propose at this juncture to enter into a discussion on this problem, and will limit myself to the consideration of the relief of the mechanical obstruction caused by a lower polar or aberrant artery, and other speakers will, no doubt, discuss the other aspect later.

I have had practical experience of most of the operations recommended for the treatment of the condition. As the disadvantages and dangers of these procedures are well known, I shall only mention them briefly. They are:

(1) *Those in which the basic principle is the division of the vessel.*—Infarction of the kidney if the divided vessel is large, with a liability to infection, particularly if the urine is infected. The loss of valuable kidney tissue—a serious matter if the other kidney is diseased.

(2) *Some form of plastic operation on the pelvis with division of the uretero-pelvic continuity.*—The risk of imperfect drainage with persistence of infection which may have previously existed or been introduced through the drainage tubes, splint catheters, &c. Stenosis of the ureter with fistula formations, &c.

The dangers of the standard operations are greatly increased when they are carried out on a solitary hydronephrotic kidney resulting from a large obstructing lower polar or aberrant artery.

The advantages of the operation to be described are: (1) All cases worthy of conservative surgery may be treated by this method. (2) There is no interference with the uretero-pelvic continuity and blood supply. (3) There is no risk of introducing infection from the skin into the urinary tract, for no drainage tube is inserted into the kidney or pelvis—indeed,

---

[1] Paper illustrated by a colour film.

He suggested that the division of bladder injuries into extra- and intraperitoneal should be dispensed with as it has no surgical significance.

The incision down to the injured bladder must be mid-line, suprapubic and transperitoneal, though the peritoneum can, of course, be closed immediately, if this surface of the bladder is found to be intact.

The use of the indwelling catheter is to be condemned and all except 4 of Mr. Parker's cases were evacuated from the forward area with suprapubic drainage only.

One of these 4 cases had a floating bladder for which a perurethral de Pezza tube was used as an aid to anchoring the bladder down in the hope of shortening the stricture which is likely to occur in such cases.

Satisfactory hæmostasis in injuries round the bladder base is sometimes very difficult to obtain, and it is better to resort to extensive packing of the extravesical space, than to catch up lumps of tissue with transfixion stitches, as with gross injury and distortion it is quite impossible to make out the position of the ureters.

The differential diagnosis between low bladder and prostatic injuries is sometimes difficult though not very important. Blood oozing out of the urethra, independent of micturition, may only mean that the external sphincter is temporarily out of action, and the actual injury may be above this level, as, in the case of high-velocity missile injuries, there is always some local concussion and loss of muscular function. Hæmorrhage and systemic shock are often very severe in these cases.

In connexion with the diagnosis of these prostatic and bladder base injuries, there is a physical sign of some importance which can be elicited on rectal examination.

The profuse hæmorrhage which nearly always occurs fills the periprostatic space and the space of Denonvilliers; consequently the examining finger will only feel a soft tender mass of blood, where the prostate ought to be, or, what is even more helpful, the prostate may be felt to be mobile and placed much higher than normally, owing to disruption from its attachments to the trigone.

When the pelvic girdle and the rectum have been injured, late sepsis and secondary hæmorrhage must be only too common in these cases, and the removal of obvious bony splinters and foreign bodies, combined with provision for very free drainage, is very essential, and much easier to accomplish at the first operation than subsequently.

Finally Mr. Parker emphasized the importance of conservative surgery in the treatment of war injuries of the external genitalia by the careful undercutting of skin flaps and preservation of all viable remaining tissue and the avoidance of tension. Some of the very grossest injuries could be successfully repaired from the point of view of sexual as well as urinary function.

Mr. John Everidge: I would like to pay an especial tribute to Mr. Poole-Wilson, having seen a number of his cases who were sent to my wards on their return to England. First-hand information reaching me from another source describing the unceasing personal attention he gave to each of his cases would explain his excellent results.

The urological beds at Horton (E.M.S.) Hospital under my care received upwards of one hundred cases of traumas of the urinary tract. A considerable number were primary from enemy action—bombs and rocket bombs—an equally large number from accidental injuries, especially ruptured bladders and urethras from fractured pelves from road transport injuries. The rest were secondary from overseas, the majority from the N. European front.

Methods adopted by the former speakers are of the standard type practised by most urological surgeons. I would, however, question Mr. Mogg's advice as to searching for and suturing extraperitoneal ruptures of the bladder. Except for an anterior tear—easily reached and useful, after partial suture, as a site for drainage—I would consider it wiser to leave any lateral tears to look after themselves; their edges will fall together and heal readily if perfect drainage is established. Suture of lateral and posterior tears from their inaccessibility is a difficult undertaking and dangerous in the reduced state of a typical case, the victim of a very serious and probably complicated injury. A finger should always explore the bladder for missiles or displaced bone. In every battle casualty and in most accidental injuries where there is the slightest suspicion of bladder or urethral injury suprapubic drainage should be established at the earliest possible moment. The good results from every front amply bore this out. One glaring exception reached me from overseas three weeks after injury: a blast dislocation and wide separation of the symphysis pubis. In spite of early suprapubic exploration a ruptured bladder was overlooked and urethral catheter drainage alone was adopted. On arrival the soldier was profoundly toxic and presented extravasation abscesses in the abdominal muscles, the right groin and the perineum. I found a very low tear in the anterior wall of the bladder. With ample suprapubic drainage and evacuation of the abscesses and with the aid of blood transfusions and courses of penicillin a good recovery was eventually made.

By the way, in these midline extraperitoneal ruptures, so common a complication of a separated symphysis, union at the symphysis may be delayed although good apposition may have been accomplished by suitable orthopædic measures, preferably, in my experience, by the pelvic sling. One of my cases on starting to walk three months after injury had a sharp hæmaturia. Cystoscopy showed blood coming from a linear tear in the scar on the anterior wall of the bladder. An X-ray photograph revealed that the pubic bones hitherto in contact were separated again.

In another case, I operated for a gross hydronephrosis—20 ounces of urine were aspirated from the kidney. The patient was five months' pregnant at the time, and has since given birth to a full-time child. She is now free from symptoms, the urine is sterile, and X-rays show a fair function.

In two other cases recently performed, a horseshoe kidney was present, and the operation worked satisfactorily even in these cases, and the patients up to the present have been entirely free from symptoms and the urine sterile.

REFERENCES

1 *Principle. See* Stewart, H. Hamilton (1947) Description of operation technique, pyelograms, &c. are to be found in the *British Journal of Surgery*, 35, 51.

2 Kelly, H. A., and Burnam, C. F. (1914) Diseases of the Kidneys, Ureters and Bladder, 1, 125. New York.

Mr. H. P. Winsbury-White showed on the screen an illustration published by the late Andrew Fullerton of a kidney showing what happened to the lower pole when its artery of supply was divided. The lower pole was in a state of necrosis. Since seeing that illustration and reading reports of a number of cases of gangrene he had given attention when dividing that vessel to amputating the lower pole of the kidney as well, and that was an operation which gave excellent results and one which he could recommend to those who had not tried it. The convalescence was particularly satisfactory. He believed that obstruction of the ureter by a blood-vessel occurred as a complication rather than as a primary cause of the hydronephrosis. His reason for this opinion was that many years ago he went round the pathological museums in London and collected all the specimens of hydronephrosis he could find in which it was shown that the ureter was obstructed by a blood-vessel which still remained intact. He found 12 altogether, and in 11 it was obvious that the obstructing vessel was the normal inferior branch of the renal artery or vein (*Brit. J. Surg.*, 1925, 13, 247; *Trans. Amer. Ass. gen.-urin. Surg.*, 1936, 29, 381).

Mr. Winsbury-White went on to say that the question as to whether or not this obstructing vessel was the cause or a complication was not entirely academic, because after dividing the vessel one must not expect to have cured the condition, if one had left behind the original cause of the hydronephrosis. There was no doubt about the relief of symptoms on dividing the vessel; it was quite dramatic. His experience with a variety of plastic procedures was that very good results were obtained in the early part of the convalescence, but the long-term results had not been good at all, and his feeling was that plastic operations as a whole were very unsatisfactory. He agreed that there were odd cases which were satisfactory, and what he had said applied also to the relief of hydronephrosis by dividing the obstructing blood-vessel. There was a significant lack in the literature concerning long-term good results in plastic operations for hydronephrosis. The fundamental point was that such patients were lucky if the opposite kidney was quite normal, and the surgeon was free, therefore, to do a nephrectomy. Mr. Winsbury-White showed a number of illustrations to demonstrate the mechanism of the obstruction by a normal renal blood-vessel when it occurred as a complication of the hydronephrosis. Several of these showed that the vein was the obstructing vessel. He showed other illustrations which indicated that the renal fascia also contributed to the obstruction of the ureter.

[*May* 22, 1947]

Clinico-Pathological Meeting Held at St. Thomas's Hospital, London, S.E.1.

The following cases and specimens were shown:

(1) Two Cases of Imperfect Descent of the Testicle. (2) Unusual Ulcer of the Bladder. (3) Transurethral Resection in a Patient of 80. (4) Tumour for Diagnosis. (5) Bladder Neck Dysfunction.—Mr. T. W. Mimpriss and Mr. St. J. M. C. Birt.

(1) Carcinoma of the Bladder: Total Cystectomy. (2) Giant Ureteric Calculus. (3) Congenital Bilateral Hydronephrosis.—Mr. Geoffrey E. Parker.

(1) Hypernephroma. (2) Tuberculous Kidney Showing Extensive Calcification. (3) Giant Ureteric Calculi. (4) Ectopic Kidney with Pyuria. (5) Intracapsular Nephrectomy for Recurrent Renal Calculi. (6) Tuberculous Kidney. (7) Carcinoma of the Prostate and Carcinoma of the Colon. *(8) Carcinoma of the Bladder Treated by Local Operation. (9) Ureteric Trans*plantation for Obstetrical Injury. (10) Ureteric Transplantation and Cystectomy for Carcinoma. (11) Transurethral Resection in a Man of 80. (12) Renal Calculus.—Mr. R. H. O. B. Robinson, Mr. T. W. Mimpriss and Mr. W. W. Wiggins-Davies.

[*June* 26, 1947]

The following cases and specimens were shown:

Kidney with Triple Pelvis and Large Ureteric Calculus.—Mr. E. W. Riches.

(1) Congenital Hydronephrosis in a Child aged 4½ Years.—Mr. I. H. Griffiths for Mr. E. W. Riches. (2) Congenital Hydronephrosis of Unusual Type.—Mr. T. H. Cullen for Mr. E. W. Riches.

neither pelvis nor kidney is opened (except in rare cases when a needle may be used for aspiration). (4) There is no possibility of fistula formation provided the operation is carefully performed.

The first of these operations which I performed over eleven years ago was immediately successful. The patient, a young man, is in continuing good health—his urine is sterile, and a normal filling of the pelvis and calices is seen in all subsequent pyelograms. The patient was 15 years of age at the time of operation. The major part of the kidney received its blood supply from the lower polar artery, making division of the latter impracticable.

Encouraged by this initial success, I used the operation at first for cases similar to the original one, with large polar arteries which I dare not divide, but presently, as these continued to give uniformly successful results, I extended its use to all cases judged worthy of conservative surgery.

Principle [1].—At a later date I realized that in the operation I had attempted to reverse certain anatomical changes which had occurred with growth. The vessels entering the kidney following the operation had the relationship which existed in infancy.

I had noticed when operating upon infants at the Children's Hospital, that they possessed kidneys which were rounded in shape, and when studying the literature I found a reference to this fact in Kelly and Burnam's [2] book. They comment on the change of shape in the kidney as it attains adult size. The shape of the kidney in the infant is such that the poles approach each other closely over an intrarenal pelvis. In early life, therefore, I believe accessory renal vessels lie close to the main renal artery, a position in which they are not likely to obstruct and prevent the escape of urine.

As the child grows, the kidney opens out "rather like a bud developing into a flower". The lower polar or aberrant artery is carried away by the diverging poles of the kidney, and in this lower position has a relationship to ureter or pelvis enabling it to produce obstruction. Thus, a lower polar vessel may not cause obstruction in the infant, but may do so in childhood or adult life. One may say that a lower polar artery should not produce obstruction unless the kidney has assumed its adult reniform shape, or the kidney is congenitally abnormal as in a horseshoe kidney.

The main principle of the operation is to mould the kidney so that the lower polar or aberrant artery is no longer capable of causing obstruction. It is brought into close relationship with the renal artery. The capsule is dissected from the anterior surfaces of the poles, but allowed to remain attached along the convex border. The poles of the kidney are then brought together, but in order to maintain them in this new position, a second folding of the kidney is necessary. The anterior surfaces of the poles are brought together so that a broad and secure grip is obtained and adhesions will develop over a broad area. The kidney is held in its new shape until adhesions develop by: (1) Hardened catgut tape passed under the capsule around the *new* convex border of the kidney rather like a rim round a wheel, and tied or sutured on the medial aspect. (2) Plain catgut sutures 4/0 through the poles. (3) Suture of the dissected flaps of capsule.

Any adhesions or minute vessels tending to retain the kink in the ureter or in the region of the uretero-pelvic junction are divided.

The pelvis, if it has been considerably distended, is plicated in front and behind by 6/0 catgut (10 day). The sutures should not penetrate the lumen. They should be placed mainly across the long axis of the pelvis, but near the pelvi-ureteric junction a few may be placed in the long axis.

Follow-up X-rays have shown that the kidney retains its new shape permanently. The lowest major calix, as a result of the moulding, occupies a higher position, and the calices, in pyelograms, tend to assume the configuration of the petals of a flower.

Results.—I have performed 21 operations and all of them have given excellent results in that the patient has been freed from symptoms. Radiological evidence has shown that the kidneys drained satisfactorily; and the urine was free from infection. In none of these cases did a congenital stricture co-exist.

The following cases are of particular interest:

A patient aged 65 suffered from fairly severe hydronephrosis due to an aberrant artery. Her other kidney had been destroyed many years before, presumably from the same condition. An operation on this kidney was the supreme test as I did not know how soon after the operation the kidney would function. The aberrant artery was of large size and following the operation described the kidney functioned immediately; 17, 34 and 74 ounces of urine were secreted in the three post-operative days without the use of intravenous therapy. Thus, the moulding of the kidney did not cause it to cease functioning.

In another case, I operated for a gross hydronephrosis—20 ounces of urine were aspirated from the kidney. The patient was five months' pregnant at the time, and has since given birth to a full-time child. She is now free from symptoms, the urine is sterile, and X-rays show a fair function.

In two other cases recently performed, a horseshoe kidney was present, and the operation worked satisfactorily even in these cases, and the patients up to the present have been entirely free from symptoms and the urine sterile.

REFERENCES

1 *Principle. See* STEWART, H. HAMILTON (1947) Description of operation technique, pyelograms, &c. are to be found in the *British Journal of Surgery*, 35, 51.
2 KELLY, H. A., and BURNAM, C. F. (1914) Diseases of the Kidneys, Ureters and Bladder, 1, 125. New York.

Mr. H. P. Winsbury-White showed on the screen an illustration published by the late Andrew Fullerton of a kidney showing what happened to the lower pole when its artery of supply was divided. The lower pole was in a state of necrosis. Since seeing that illustration and reading reports of a number of cases of gangrene he had given attention when dividing that vessel to amputating the lower pole of the kidney as well, and that was an operation which gave excellent results and one which he could recommend to those who had not tried it. The convalescence was particularly satisfactory. He believed that obstruction of the ureter by a blood-vessel occurred as a complication rather than as a primary cause of the hydronephrosis. His reason for this opinion was that many years ago he went round the pathological museums in London and collected all the specimens of hydronephrosis he could find in which it was shown that the ureter was obstructed by a blood-vessel which still remained intact. He found 12 altogether, and in 11 it was obvious that the obstructing vessel was the normal inferior branch of the renal artery or vein (*Brit. J. Surg.*, 1925, 13, 247; *Trans. Amer. Ass. gen.-urin. Surg.*, 1936, 29, 381).

Mr. Winsbury-White went on to say that the question as to whether or not this obstructing vessel was the cause or a complication was not entirely academic, because after dividing the vessel one must not expect to have cured the condition, if one had left behind the original cause of the hydronephrosis. There was no doubt about the relief of symptoms on dividing the vessel; it was quite dramatic. His experience with a variety of plastic procedures was that very good results were obtained in the early part of the convalescence, but the long-term results had not been good at all, and his feeling was that plastic operations as a whole were very unsatisfactory. He agreed that there were odd cases which were satisfactory, and what he had said applied also to the relief of hydronephrosis by dividing the obstructing blood-vessel. There was a significant lack in the literature concerning long-term good results in plastic operations for hydronephrosis. The fundamental point was that such patients were lucky if the opposite kidney was quite normal, and the surgeon was free, therefore, to do a nephrectomy. Mr. Winsbury-White showed a number of illustrations to demonstrate the mechanism of the obstruction by a normal renal blood-vessel when it occurred as a complication of the hydronephrosis. Several of these showed that the vein was the obstructing vessel. He showed other illustrations which indicated that the renal fascia also contributed to the obstruction of the ureter.

[*May* 22, 1947]

CLINICO-PATHOLOGICAL MEETING HELD AT ST. THOMAS'S HOSPITAL, LONDON, S.E.1.

THE following cases and specimens were shown:

(1) Two Cases of Imperfect Descent of the Testicle. (2) Unusual Ulcer of the Bladder. (3) Transurethral Resection in a Patient of 80. (4) Tumour for Diagnosis. (5) Bladder Neck Dysfunction.—Mr. T. W. MIMPRISS and Mr. ST. J. M. C. BIRT.

(1) Carcinoma of the Bladder: Total Cystectomy. (2) Giant Ureteric Calculus. (3) Congenital Bilateral Hydronephrosis.—Mr. GEOFFREY E. PARKER.

(1) Hypernephroma. (2) Tuberculous Kidney Showing Extensive Calcification. (3) Giant Ureteric Calculi. (4) Ectopic Kidney with Pyuria. (5) Intracapsular Nephrectomy for Recurrent Renal Calculi. (6) Tuberculous Kidney. (7) Carcinoma of the Prostate and Carcinoma of the Colon. (8) Carcinoma of the Bladder Treated by Local Operation. (9) Ureteric Transplantation for Obstetrical Injury. (10) Ureteric Transplantation and Cystectomy for Carcinoma. (11) Transurethral Resection in a Man of 80. (12) Renal Calculus.—Mr. R. H. O. B. ROBINSON, Mr. T. W. MIMPRISS and Mr. W. W. WIGGINS-DAVIES.

[*June* 26, 1947]

THE following cases and specimens were shown:

Kidney with Triple Pelvis and Large Ureteric Calculus.—Mr. E. W. RICHES.

(1) Congenital Hydronephrosis in a Child aged 4½ Years.—Mr. I. H. GRIFFITHS for Mr. E. W. RICHES. **(2) Congenital Hydronephrosis of Unusual Type.**—Mr. T. H. CULLEN for Mr. E. W. RICHES.

(1) True Hypernephroma of Adrenal Origin. (2) Actinomycosis of Testicle.—Mr. HOWARD G. HANLEY.

Calcification of Kidney and Ureter (X-rays).—Mr. J. H. CARVER.

(1 and 2) Cysts in the Lower Lobe of the Kidney. (3) Unusual Tumour of the Bladder (A Granuloma).—Mr. HAROLD DODD.

(1) Pyelonephritis with Multiple Cortical Abscess Formation in a Kidney with Double Pelvis and Ureter. (2) Calcified Left Kidney with Ureter and Two Dense Calcified Foci in the Middle Zone of the Left Lung.—Mr. R. S. MURLEY.

Gunshot Wound of the Ureter.—Mr. ANDREW M. DESMOND (introduced by Mr. H. K. VERNON).

Advanced Carcinoma of the Bladder Excised by Perineo-abdominal Cystectomy (Hydronephrosis and Pyonephrosis).—Mr. ALAN HUNT (Specimen shown by Mr. S. O. AYLETT).

Epididymoma; Histology: Old Hæmatoma.—Mr. A. WILFRID ADAMS.

Survival of a Testicle Transplanted into Scarpa's Triangle.—R. OGIER WARD, D.S.O., M.Ch.

August 1934: The patient was a boy aged 9. He was inclined to general obesity particularly of the buttocks. The pelvis appeared unduly wide. The scrotum was undeveloped. The left testicle could not be felt, the right was palpable in the inguinal canal and could just be pushed into the upper scrotum; it was very small. Operative treatment had already been advised by another surgeon but refused.

March 1936: He had been examined four times during the intervening period. Pregnyl had been tried, but there had been no improved development. A right orchidopexy was performed (Keetley-Torek technique). The testicle was minute (about 0·7 cm.) enveloped in deep subcutaneous fat.

August 1936: The second stage of the operation performed; this was difficult because of the excess of fat.

April 1937: It seemed that the right testicle had atrophied completely. The left testicle could be felt in the scrotum, it was very small.

June 1945: Now aged 20, average size and normal development. Left testicle was in the scrotum and normal. Sexual characteristics quite normal. To my surprise I found in Scarpa's triangle on the right side a swelling the size of a normal testicle.

July 1945: Exploration of Scarpa's triangle revealed a testicle two-thirds the size of the left one. Two pieces excised for microscopy (Dr. T. Joekes) showed rete testis and seminiferous tubules but no evidence of spermatogenesis.

It was considered most unlikely that any further reconstruction could be carried out successfully but as it seemed unwise to leave the testicle in the thigh an attempt was made to rejoin the right cord and epididymis to it. When, however, five months later the testicle was restored to the scrotum complete atrophy followed.

Comment.—It is obvious that in the operation of August 1936, owing to the minute size of the testicle and the excess of fat, the plane of dissection had passed between the epididymis and the testis, leaving the latter in the thigh. It is remarkable that the organ had there acquired a blood supply sufficient for it to develop to above twenty times its size.

Section of Experimental Medicine and Therapeutics

with the Medical Society for the Study of Venereal Diseases

Chairman—E. N. ALLOTT, F.R.C.P.

[*July* 17, 1947]

DISCUSSION ON THE TREATMENT OF SYPHILIS WITH PENICILLIN

Dr. Joseph Earle Moore, U.S.A.: I propose to give you a brief account of the American experience with penicillin in syphilis. Treatment has been conducted on an organized co-operative basis under the auspices of the Committee of Medical Research and later under the Research Grants Division, National Institute of Public Health of the United States Public Health Service. The information from the clinics and Services collaborating in this work was reported on standard forms in a central statistical unit and analysed by the Department of Biostatistics of the Johns Hopkins School of Hygiene and Public Health. We now have data on 40,000 cases of early syphilis and a smaller but substantial number of cases in various phases of late syphilitic infection.

In addition to tne clinics co-operating in this experiment there are also eight laboratories collaborating in the study of the use of penicillin in rabbit syphilis. From their work it appears that penicillin G is superior in treponemicidal effect to X, F or K. This is in contrast to the bactericidal effects of these penicillins against certain other organisms. Penicillin X is two to ten times superior to G in *gonococcal*, *staphylococcal* and *pneumococcal* infections. In syphilitic rabbits, however, G is about six times as effective as F or X and about twenty times superior to penicillin K. It is fortunate that commercial penicillins have been composed predominantly of penicillin G and it is the easiest to prepare in relatively pure crystalline form. The other species F, dihydro F, X and K, have been available in pure form only in very small amounts for experimental study. Other antibiotic agents, in particular streptomycin and bacitracin, have not been shown to equal the effect of penicillin G.

Penicillin cures syphilis in rabbits whether the animals are treated early (within six weeks after infection) or late (six months or later after infection). Many small doses are more effective than one or a few large doses. The curative dose is related also to the duration of infection. In animals treated within four hours to four days after inoculation, therefore, before the appearance of a chancre, far less penicillin is required (total dosage) than if treatment is delayed for six weeks or longer. The results in animals are likewise related to the size of the inoculum. Animals treated soon after the injection of 2 to 20 organisms require a smaller total dose for cure than if the inoculation is a large one. Cure is accomplished within the actual period of treatment since treated animals with healing chancres still present may be reinfected as soon as four days after the completion of treatment. These facts raised the possibility of the prophylactic use of penicillin by means of oral administration. The U.S. Army and Navy have now in progress controlled experiments in selected units in which 500,000 units of penicillin administered by mouth in personnel sexually exposed is being tried for prophylactic effect.

(1) True Hypernephroma of Adrenal Origin. (2) Actinomycosis of Testicle.—Mr. HOWARD G. HANLEY.

Calcification of Kidney and Ureter (X-rays).—Mr. J. H. CARVER.

(1 and 2) Cysts in the Lower Lobe of the Kidney. (3) Unusual Tumour of the Bladder (A Granuloma).—Mr. HAROLD DODD.

(1) Pyelonephritis with Multiple Cortical Abscess Formation in a Kidney with Double Pelvis and Ureter. (2) Calcified Left Kidney with Ureter and Two Dense Calcified Foci in the Middle Zone of the Left Lung.—Mr. R. S. MURLEY.

Gunshot Wound of the Ureter.—Mr. ANDREW M. DESMOND (introduced by Mr. H. K. VERNON).

Advanced Carcinoma of the Bladder Excised by Perineo-abdominal Cystectomy (Hydronephrosis and Pyonephrosis).—Mr. ALAN HUNT (Specimen shown by Mr. S. O. AYLETT).

Epididymoma; Histology: Old Hæmatoma.—Mr. A. WILFRID ADAMS.

Survival of a Testicle Transplanted into Scarpa's Triangle.—R. OGIER WARD, D.S.O., M.Ch.

August 1934: The patient was a boy aged 9. He was inclined to general obesity particularly of the buttocks. The pelvis appeared unduly wide. The scrotum was undeveloped. The left testicle could not be felt, the right was palpable in the inguinal canal and could just be pushed into the upper scrotum; it was very small. Operative treatment had already been advised by another surgeon but refused.

March 1936: He had been examined four times during the intervening period. Pregnyl had been tried, but there had been no improved development. A right orchidopexy was performed (Keetley-Torek technique). The testicle was minute (about 0·7 cm.) enveloped in deep subcutaneous fat.

August 1936: The second stage of the operation performed; this was difficult because of the excess of fat.

April 1937: It seemed that the right testicle had atrophied completely. The left testicle could be felt in the scrotum, it was very small.

June 1945: Now aged 20, average size and normal development. Left testicle was in the scrotum and normal. Sexual characteristics quite normal. To my surprise I found in Scarpa's triangle on the right side a swelling the size of a normal testicle.

July 1945: Exploration of Scarpa's triangle revealed a testicle two-thirds the size of the left one. Two pieces excised for microscopy (Dr. T. Joekes) showed rete testis and seminiferous tubules but no evidence of spermatogenesis.

It was considered most unlikely that any further reconstruction could be carried out successfully but as it seemed unwise to leave the testicle in the thigh an attempt was made to rejoin the right cord and epididymis to it. When, however, five months later the testicle was restored to the scrotum complete atrophy followed.

Comment.—It is obvious that in the operation of August 1936, owing to the minute size of the testicle and the excess of fat, the plane of dissection had passed between the epididymis and the testis, leaving the latter in the thigh. It is remarkable that the organ had there acquired a blood supply sufficient for it to develop to above twenty times its size.

the drug is used alone or with arsenic. This may be of some importance to the mass treatment of syphilis in that an adjuvant total dose of bismuth adequate to prevent relapses over the first nine to twelve months may allow the patient to develop enough immunity so that he is infectious for others for a shorter time than would otherwise be the case.

The results on the whole indicate that the failure rate of treatment with penicillin in patients with early syphilis after eighteen to twenty-four months of observation is, with the treatment systems which we have employed, in the general range of 25 to 35%. The failure rate was not materially improved upon by the addition of either arsenic or bismuth or both in the doses we employed, nor were the results materially improved upon by fever. These are results which are substantially worse than the best obtainable by metal chemotherapy without penicillin, when the failure rate may be as low as 3 to 10%, *provided the patient completes the treatment and is not seriously ill or killed as a result of it.* With metal chemotherapy, if treatment is completed within a brief period of time, the mortality rate from treatment *per se* is excessive, whereas if it is prolonged for the sake of safety comparatively few patients can be held to the conclusion of treatment. Penicillin, however, offers the advantage of complete safety when used within the time limits of practicability, which is, with penicillin in aqueous solution, about fifteen days. This is the maximum time for which we can hold patients in hospital. On the other hand, the results are such as to indicate that for the individual patient they may be poor, that is, less than can be accomplished with metal chemotherapy alone.

Penicillin resistance has not been observed in syphilis in man.

This information raises a number of fundamental questions. Why is early syphilis apparently uniformly curable in the rabbit, whereas in man there is a substantial residue of failure? Is this related to the number of treponemes to be destroyed or to some factor of tissue localization in man but not in animals, or some factor of immunity? Is man dependent on the development of resistance against the few treponemes not destroyed in the first massive attack? What is the significance of low titre seroresistance after penicillin? Does it represent persistence of treponemes or their tissue reaction or a persistence of immunity after cure? Can any evidence be evolved to differentiate relapse and reinfection? While with other organisms penicillin is effective only when the organisms are in a rapidly dividing state, it has so far not been possible to work out the time-dose factor in relation to the rate of multiplication of the treponemes, and the question of the value of repeated courses of penicillin in peanut oil–beeswax is still to be solved. Further it is still unknown how long seronegativity must continue before the patient can be discharged from further investigation.

Now, in contrast to a failure rate of 25% or more in patients with acquired early syphilis, penicillin is spectacularly and nearly completely successful in the prevention of prenatal syphilis by treatment of the pregnant syphilitic mother. The failure rate in the infant is only 1 to 2%. The total dose and duration of treatment are the same as in early syphilis. Why is it that the fœtus with a massive and overwhelming infection is cured by a substantially lower concentration than in its mother and which fails to cure the parent? The fœtus may be influenced favourably even when treatment is not begun till the eighth or ninth month.

The action of penicillin in congenital syphilis raises a similar problem. Penicillin has not reduced the mortality rate but most of the deaths in such infants are neither due to syphilis *per se* nor the Herxheimer reaction, but are due to other infections or nutritional disturbances. In infants which survive the treatment the failure rate is substantially lower than the adult rate and the clinical relapse rate is only about one-sixth as frequent. Why, again, are areas packed with treponemes more susceptible to penicillin? Is it due to difference in infantile and adult tissue localization or to unidentified immunity factors which may vary in the infant as contrasted with the adult?

In latent and late syphilis other than neurosyphilis penicillin heals lesions if any are present, but has no greater effect on the blood serologic test than has any other form of treatment. Nothing can be said of the eventual clinical outcome in these cases, since years of post-treatment observation are necessary to determine the point. In patients with latent syphilis, what matters is what happens to the patient, not what happens to his blood test and it is necessary to follow large series of patients quite literally for a lifetime.

In cardiovascular syphilis, the most that can be said of penicillin to date is that, whether initiated with large or small doses, it appears to do no harm. The Herxheimer reaction, so-called therapeutic shock, need not be greatly feared. At the Johns Hopkins Hospital we have now treated some fifty patients with saccular aneurysms or aortic regurgitation, dividing them into two groups, one treated initially with 1,000 units gradually increased to an average therapeutic dosage: the other treated with 50,000 to 100,000 units from the start. In neither group was there any evidence of damage to the patients detectable by clinical symptoms, electrocardiograms, sedimentation rates, temperature, leucocyte count, &c. No

In experimental animals, neither *in vitro* against cultured non-pathogenic strains of spirochætes nor *in vivo* has there appeared any definite evidence of penicillin resistance. The effect of penicillin in animals is apparently enhanced by the simultaneous administration of oxophenarsine hydrochloride (mapharside). The effect is likewise enhanced, in an additive sense, by the simultaneous administration of bismuth. The drug is more effective when administered at fever temperature than at normal body temperature.

In early acquired infection in man, if freedom from relapse and prolonged seronegativity up to three years after treatment indicate cure of early syphilis, then penicillin is also curative, but by no means so uniformly as in the experimental animal. In our study of the results of treatment, patients have been classified as failures if at any time after treatment there has been evidence of clinical or serologic relapse or reinfection. It is clinically impossible to differentiate reinfection from relapse; even although the presumption of reinfection was very strong, all such patients were classified as treatment failures. To the extent that there is a predominance of actual reinfection over relapse, the results I shall discuss are better than indicated. Serologic relapse includes not only patients who relapse after having become sero-negative but also those whose serologic titre only temporarily drops to a low titre followed by a subsequent rise. Patients have been classified as failure when reagins are persisting in the blood one year after treatment (seroresistant).

When the cumulative failure rate was related to the total dose of penicillin given in all types of early syphilis every three hours for seven to eight days the following results were obtained: with a total dose of 300,000 units the failure rate at the end of twenty-two months approximated 50%; with 600,000 units it dropped to 35%. When the dose reached 1·2 to 4·8 mega units, there was no appreciable difference between the failure rates at the end of one year. All these experiments were done with commercially ampouled penicillin which will have an expected quantitative error of dosage between −15 and +40%. Related to the duration of treatment a total of 2·4 million units given every three hours over periods of four, seven-and-a-half and fifteen days the cumulated failure rates at the end of nearly two years showed no difference. When the total duration of treatment remains standard at four days and the total dose 1·2 million units given at either three or six hour intervals there was no difference in the cumulative failure rates. In a small group when twenty-five million units were given by continuous intravenous drip in one day the failure rate approximated to 60% at the end of six months! There appears to be no statistically significant difference in therapeutic efficiency between penicillin of relatively low potency and penicillin of comparatively higher potency, 900 units or more per mgm.

In another series 1·2 million units of penicillin were given for seven and a half days combined with these different adjuvants, namely arsenic, bismuth or fever. Of these last, one group was treated with penicillin plus fever in four days, the other group in seven days. There appears to be no material advantage to human beings of a combination of penicillin with bismuth or arsenic, in the dosages and within the time limits in which these drugs were used. A total dose of 480 mg. of auxiliary mapharside was given; of bismuth 1,000 mg. —doses in themselves known to be not curative and subject to a high relapse rate.

The results with penicillin show an obvious advantage in giving treatment early. In patients treated within the first seven days the results are materially better than when treatment is delayed until lesions have been present for from four to seven weeks, and still better than when lesions have been present for eight weeks or longer. The data are roughly separable into the clinical groups of seronegative primary syphilis (less than seven days) and early secondary syphilis (more than fifty-six days).

It seems impossible for various reasons to develop an ambulatory method of treatment with aqueous penicillin. We have therefore concentrated in the use of penicillin in peanut oil–beeswax, a formula involving the suspension of penicillin in peanut oil which contains 4·8% of purified beeswax. This may be administered once a day rather than every few hours since a detectable blood level can be obtained from a single dose of 600,000 units which lasts twenty to twenty-four hours. Patients have been so treated with three different systems; one with the administration of 600,000 units penicillin daily for eight days, another, daily injections of 600,000 units for sixteen days and the third by twice-weekly injections, given over eight weeks to a total of sixteen injections. The results with these systems are relatively indistinguishable. The data further suggest that at the end of twelve to twenty-four months the results from penicillin in peanut oil–beeswax are as good as, and may be better than may be expected from penicilllin in aqueous solution. This is being confirmed by still further observations. The incidence of clinical relapse, including reinfection, is about the same, regardless of how the penicillin was employed, whether the dosage was low or relatively high, and whether the drug was or was not combined with metal chemotherapy. The time of appearance of relapse when penicillin is combined with bismuth is slightly later than when the drug is used alone or with arsenic. This may be of some importance to the mass treatment of syphilis in that an adjuvant total dose of bismuth adequate to prevent relapses over the first nine to twelve months may allow the patient to develop enough immunity so that he is infectious for others for a shorter time than would otherwise be the case.

The results on the whole indicate that the failure rate of treatment with penicillin in patients with early syphilis after eighteen to twenty-four months of observation is, with the treatment systems which we have employed, in the general range of 25 to 35%. The failure rate was not materially improved upon by the addition of either arsenic or bismuth or both in the doses we employed, nor were the results materially improved upon by fever. These are results which are substantially worse than the best obtainable by metal chemotherapy without penicillin, when the failure rate may be as low as 3 to 10%, *provided the patient completes the treatment and is not seriously ill or killed as a result of it.* With metal chemotherapy, if treatment is completed within a brief period of time, the mortality rate from treatment *per se* is excessive, whereas if it is prolonged for the sake of safety comparatively few patients can be held to the conclusion of treatment. Penicillin, however, offers the advantage of complete safety when used within the time limits of practicability, which is, with penicillin in aqueous solution, about fifteen days. This is the maximum time for which we can hold patients in hospital. On the other hand, the results are such as to indicate that for the individual patient they may be poor, that is, less than can be accomplished with metal chemotherapy alone.

Penicillin resistance has not been observed in syphilis in man.

This information raises a number of fundamental questions. Why is early syphilis apparently uniformly curable in the rabbit, whereas in man there is a substantial residue of failure? Is this related to the number of treponemes to be destroyed or to some factor of tissue localization in man but not in animals, or some factor of immunity? Is man dependent on the development of resistance against the few treponemes not destroyed in the first massive attack? What is the significance of low titre seroresistance after penicillin? Does it represent persistence of treponemes or their tissue reaction or a persistence of immunity after cure? Can any evidence be evolved to differentiate relapse and reinfection? While with other organisms penicillin is effective only when the organisms are in a rapidly dividing state, it has so far not been possible to work out the time-dose factor in relation to the rate of multiplication of the treponemes, and the question of the value of repeated courses of penicillin in peanut oil–beeswax is still to be solved. Further it is still unknown how long seronegativity must continue before the patient can be discharged from further investigation.

Now, in contrast to a failure rate of 25% or more in patients with acquired early syphilis, penicillin is spectacularly and nearly completely successful in the prevention of prenatal syphilis by treatment of the pregnant syphilitic mother. The failure rate in the infant is only 1 to 2%. The total dose and duration of treatment are the same as in early syphilis. Why is it that the fœtus with a massive and overwhelming infection is cured by a substantially lower concentration than in its mother and which fails to cure the parent? The fœtus may be influenced favourably even when treatment is not begun till the eighth or ninth month.

The action of penicillin in congenital syphilis raises a similar problem. Penicillin has not reduced the mortality rate but most of the deaths in such infants are neither due to syphilis *per se* nor the Herxheimer reaction, but are due to other infections or nutritional disturbances. In infants which survive the treatment the failure rate is substantially lower than the adult rate and the clinical relapse rate is only about one-sixth as frequent. Why, again, are areas packed with treponemes more susceptible to penicillin? Is it due to difference in infantile and adult tissue localization or to unidentified immunity factors which may vary in the infant as contrasted with the adult?

In latent and late syphilis other than neurosyphilis penicillin heals lesions if any are present, but has no greater effect on the blood serologic test than has any other form of treatment. Nothing can be said of the eventual clinical outcome in these cases, since years of post-treatment observation are necessary to determine the point. In patients with latent syphilis, what matters is what happens to the patient, not what happens to his blood test and it is necessary to follow large series of patients quite literally for a lifetime.

In cardiovascular syphilis, the most that can be said of penicillin to date is that, whether initiated with large or small doses, it appears to do no harm. The Herxheimer reaction, so-called therapeutic shock, need not be greatly feared. At the Johns Hopkins Hospital we have now treated some fifty patients with saccular aneurysms or aortic regurgitation, dividing them into two groups, one treated initially with 1,000 units gradually increased to an average therapeutic dosage: the other treated with 50,000 to 100,000 units from the start. In neither group was there any evidence of damage to the patients detectable by clinical symptoms, electrocardiograms, sedimentation rates, temperature, leucocyte count, &c. No

one is yet prepared to offer any statement as to whether penicillin does cardiovascular syphilis any good, but since it heals visible lesions it should heal lesions which cannot be seen. In contrast to man, however, rabbits with late syphilis appear to be as readily curable with penicillin as do those with early infections. A smaller total dose of penicillin, even, may be required to cure the animals with late than with early syphilis. Is late syphilis in man curable with this drug? Only much further study will give us the information.

In syphilis of the nervous system, regardless of the clinical syndrome present, there are profound and uniform effects from penicillin administered intramuscularly. Whether in asymptomatic neurosyphilis, acute syphilitic meningitis, tabes dorsalis or general paresis, cell count and protein content are reduced to normal in practically all cases. This occurs within a few weeks and in many cases within a few days. Colloidal tests tend towards normal as protein decreases. The spinal fluid Wassermann test is also favourably though more slowly influenced; the rate of reversal of this test depends on the duration of infection with syphilis and the original complement-fixation titre of the fluid. The more strongly positive the fluid the longer it takes for the Wassermann test to become negative. These evidences of laboratory improvement, regardless of the clinical type of the disease, persist at least for three years in about 90% of cases treated: only about 10% of the total showing a later return of fluid abnormalities. There is no need for the technically difficult administration of penicillin by the subdural or intrathecal route. Clinically, penicillin appears to be superior to any form of metal chemotherapy. Regardless of the type of neurosyphilis, clinical improvement may be expected from penicillin to the extent to which symptoms and physical signs depend on inflammation rather than on degeneration. Neither penicillin nor any other form of treatment will restore dead brain cells or fibre tracts, although further destruction and clinical progression may be prevented. In certain of the relatively benign forms of neurosyphilis, penicillin alone gives satisfactory results. In the more serious forms the combination of penicillin and fever from induced malaria may be superior to penicillin alone, both from clinical and laboratory standards. The time-dosage relationship in neurosyphilis is not so clearly established as in early syphilis. Most American observers believe that a large total dose is superior to smaller dosage and that ten to twenty days' treatment is better than a short duration.

The advent of penicillin has made it possible to accomplish as much or more in most cases of neurosyphilis as previously was obtainable with fever and several years of subsequent metal chemotherapy. Its immediate effects appear to be more striking in neurosyphilis than in early syphilis. Available data indicate that penicillin penetrates the tissue of the nervous system in a concentration far lower than that of other tissues. If improvement depends on tissue concentration of the drug, why are results apparently better in neurosyphilis than early syphilis in which the nervous system is spared? Are the good results permanent?

Penicillin represents a major advance in syphilotherapy. There are still a number of curious and unexplained differences in its effect in various stages of syphilitic infection, whether the variable mixtures of commercial penicillin or crystalline penicillin G are used. It probably represents only the first faltering steps in the antibiotic therapy of this disease. Further studies may replace penicillin by a new and more powerful antibiotic. Pending such a development the organized study of penicillin has provided information within four years, which otherwise would have required a generation to accumulate. Further, the co-operative study has re-emphasized the gaps in our knowledge of the fundamental biology of syphilitic infection which must be filled in before the perfect form of treatment of syphilis can be found.

Dr. E. M. Lourie (*Director of the Department of Chemotherapy, Liverpool School of Tropical Medicine*) recalled that his original observations that penicillin was effective against spirochætoses had been made on *Spirochæta recurrentis* and *Spirillum minus* infections in mice in August 1942. Although no secret had been made of the work and its potential significance for syphilis, it did not appear in print until July and December 1943 [1, 2], that is practically simultaneously with the announcement by Mahoney *et al.* [3] that penicillin is, in fact, efficacious against syphilis. Prior to this he had tried unsuccessfully to obtain an allocation for human trials. Detailed plans had already been laid with Dr. A. O. F. Ross for trials against syphilis before Mahoney's paper had appeared, and it was by the merest coincidence that they had chosen a total dosage per case of 2·4 mega units, exactly twice that chosen by the Americans. If penicillin proved to be ineffective at maximal dosages it would then be possible to dismiss the whole subject with relatively little waste of time or penicillin, while, if effective, later effort could be devoted to determining the minimum effective dosage. The results of the first four cases of secondary syphilis he and Dr. Ross treated with 2·4 mega units [4] made them doubt whether penicillin had been as effective as arsenicals and bismuth. The concurrent investigation in the United States [5] of some 1,500 cases of early syphilis treated with 60,000 to 1·2 mega units led to a similar cautionary conclusion that "certainly the minimum dose, especially in secondary syphilis, should not be less than 1,200,000 units; probably it should be more".

It seemed to him that there had been a singular reluctance to determine whether the efficacy of penicillin could not be stepped up by a bold increase in dosage. The laboratory evidence of Eagle and Musselman [6] had been adduced against the value of massive dosage, but other laboratory work [7] had encouraged his group to find out what penicillin could do against syphilis when given in massive dosage. Dosage was such as obviated hospitalization and serious interference with the patient's daily work. They had obtained equally good results with two such courses, (i) three intramuscular doses of 500,000 units at hourly intervals for five consecutive days, or (ii) two intramuscular doses of 1,000,000 units at hourly intervals, on each of five days. The combined results of these two courses gave 87 to 92% success in twenty-four cases of primary syphilis and 76 to 92% success in fifty secondary cases. The results of the small series may not be as good as might be obtained by other forms of treatment, but they have the great virtue of having been produced by ambulatory treatment. If course (ii) were supplemented with daily injection of say 0·09 gramme neohalarsine or 0·06 gramme mapharside given in the hour between the two penicillin injections, results might be obtained as good as by any other method but involving far smaller demands on the patients' time and convenience.

He concluded by paying a tribute to the truly remarkable organization, scope and achievement of the American effort, so largely guided and inspired by Dr. Earle Moore.

REFERENCES

1 Liverpool School of Tropical Medicine, 44th Annual Report, August 1, 1942 – July 31, 1943, p. 9.
2 LOURIE, E. M., and COLLIER, H. O. J. (1943) *Ann. trop. Med. Parasit.*, 37, 200.
3 MAHONEY, J. F., ARNOLD, R. C., and HARRIS, A. (1943) *Vener. Dis. Inform.*, 24, 355.
4 ROSS, A. O. F., NELSON, R. B., LOURIE, E. M., COLLIER, H. O. J. (1944) *Lancet* (ii), 845.
5 MOORE, J. E., MAHONEY, J. F., SCHWARTZ, W. H., STERNBERG, T. H., and WOOD, W. B. (1944) *J. Amer. med. Ass.*, 126, 67.
6 EAGLE, H., and MUSSELMAN, A. D. (1944) *J. exp. Med.*, 80, 493.
7 LOURIE, E. M., COLLIER, H. O. J., ROSS, A. O. F., NELSON, R. B., ROBINSON, D. T. (1945) *Lancet* (ii), 696.

Lieut.-Colonel **J. W. Eames, R.A.M.C.**, stated that in 1944 2·4 mega units of penicillin were given in the Army with a failure rate of 8% at the end of six months. Since then further methods have been used but the follow up was difficult. In the case of patients suffering from primary syphilis treated with 2·4 mega units of penicillin (aqueous) over seven and a half days the maximum relapse incidence was in the first six months. The calculated cumulative relapse rate at twelve months for seronegative primary cases was 14% and for seropositive primary cases 13%, and for secondary cases 17·5%. In patients treated with 4 mega units over twelve and a half days, the relapse rate, as far as could be seen from the small follow-up, appeared to be essentially the same. The results of using 2·4 mega units of penicillin plus 0·6 gramme mapharside in ten days, and a similar course giving 0·4 gramme mapharside and 1 gramme bismuth did not appear to differ materially from those obtained by using penicillin alone, but the number followed up had been small. With 2·4 mega units in treatment seroresistance occurred in 3% of seropositive primary cases and 8% of secondary cases and with 4 mega units seropositive primary cases showed a resistance rate of 1·6% and secondary cases 3·8%.

Present treatment in the Army is 50,000 units penicillin three-hourly for ten days, combined with 1·35 grammes N.A.B. and 0·6 gramme bismuth in divided doses on the second, fifth and ninth day followed by 0·6 gramme N.A.B. and 0·2 gramme bismuth weekly for eight weeks. It was too early yet to evaluate this scheme. Bismuth had apparently no effect on the penicillin level of the blood.

Mr. **A. J. King** felt that now that Dr. Moore had produced the figures it was clear enough there was a considerable failure rate in cases of early syphilis with penicillin alone although such findings did not accord with his own experience. Dr. Curtis and he had limited their inquiries at the Whitechapel Clinic to those discharged soldiers who had received in the Army a total of 2·4 mega units of penicillin in sixty three-hourly injections of 40,000 units each in watery solution. Of 82 patients in this class observed over twelve months at least, in only 4 had treatment failed. This was a very small group and he hoped that other medical officers at other clinics would make similar investigations to obtain a large number of cases observed for a long period.

one is yet prepared to offer any statement as to whether penicillin does cardiovascular syphilis any good, but since it heals visible lesions it should heal lesions which cannot be seen. In contrast to man, however, rabbits with late syphilis appear to be as readily curable with penicillin as do those with early infections. A smaller total dose of penicillin, even, may be required to cure the animals with late than with early syphilis. Is late syphilis in man curable with this drug? Only much further study will give us the information.

In syphilis of the nervous system, regardless of the clinical syndrome present, there are profound and uniform effects from penicillin administered intramuscularly. Whether in asymptomatic neurosyphilis, acute syphilitic meningitis, tabes dorsalis or general paresis, cell count and protein content are reduced to normal in practically all cases. This occurs within a few weeks and in many cases within a few days. Colloidal tests tend towards normal as protein decreases. The spinal fluid Wassermann test is also favourably though more slowly influenced; the rate of reversal of this test depends on the duration of infection with syphilis and the original complement-fixation titre of the fluid. The more strongly positive the fluid the longer it takes for the Wassermann test to become negative. These evidences of laboratory improvement, regardless of the clinical type of the disease, persist at least for three years in about 90% of cases treated: only about 10% of the total showing a later return of fluid abnormalities. There is no need for the technically difficult administration of penicillin by the subdural or intrathecal route. Clinically, penicillin appears to be superior to any form of metal chemotherapy. Regardless of the type of neurosyphilis, clinical improvement may be expected from penicillin to the extent to which symptoms and physical signs depend on inflammation rather than on degeneration. Neither penicillin nor any other form of treatment will restore dead brain cells or fibre tracts, although further destruction and clinical progression may be prevented. In certain of the relatively benign forms of neurosyphilis, penicillin alone gives satisfactory results. In the more serious forms the combination of penicillin and fever from induced malaria may be superior to penicillin alone, both from clinical and laboratory standards. The time-dosage relationship in neurosyphilis is not so clearly established as in early syphilis. Most American observers believe that a large total dose is superior to smaller dosage and that ten to twenty days' treatment is better than a short duration.

The advent of penicillin has made it possible to accomplish as much or more in most cases of neurosyphilis as previously was obtainable with fever and several years of subsequent metal chemotherapy. Its immediate effects appear to be more striking in neurosyphilis than in early syphilis. Available data indicate that penicillin penetrates the tissue of the nervous system in a concentration far lower than that of other tissues. If improvement depends on tissue concentration of the drug, why are results apparently better in neurosyphilis than early syphilis in which the nervous system is spared? Are the good results permanent?

Penicillin represents a major advance in syphilotherapy. There are still a number of curious and unexplained differences in its effect in various stages of syphilitic infection, whether the variable mixtures of commercial penicillin or crystalline penicillin G are used. It probably represents only the first faltering steps in the antibiotic therapy of this disease. Further studies may replace penicillin by a new and more powerful antibiotic. Pending such a development the organized study of penicillin has provided information within four years, which otherwise would have required a generation to accumulate. Further, the co-operative study has re-emphasized the gaps in our knowledge of the fundamental biology of syphilitic infection which must be filled in before the perfect form of treatment of syphilis can be found.

Dr. E. M. Lourie (*Director of the Department of Chemotherapy, Liverpool School of Tropical Medicine*) recalled that his original observations that penicillin was effective against spirochætoses had been made on *Spirochæta recurrentis* and *Spirillum minus* infections in mice in August 1942. Although no secret had been made of the work and its potential significance for syphilis, it did not appear in print until July and December 1943 [1, 2], that is practically simultaneously with the announcement by Mahoney *et al.* [3] that penicillin is, in fact, efficacious against syphilis. Prior to this he had tried unsuccessfully to obtain an allocation for human trials. Detailed plans had already been laid with Dr. A. O. F. Ross for trials against syphilis before Mahoney's paper had appeared, and it was by the merest coincidence that they had chosen a total dosage per case of 2·4 mega units, exactly twice that chosen by the Americans. If penicillin proved to be ineffective at maximal dosages it would then be possible to dismiss the whole subject with relatively little waste of time or penicillin, while, if effective, later effort could be devoted to determining the minimum effective dosage. The results of the first four cases of secondary syphilis he and Dr. Ross treated with 2·4 mega units [4] made them doubt whether penicillin had been as effective as arsenicals and bismuth. The concurrent investigation in the United States [5] of some 1,500 cases of early syphilis treated with 60,000 to 1·2 mega units led to a similar cautionary conclusion that "certainly the minimum dose, especially in secondary syphilis, should not be less than 1,200,000 units; probably it should be more".

It seemed to him that there had been a singular reluctance to determine whether the efficacy of penicillin could not be stepped up by a bold increase in dosage. The laboratory evidence of Eagle and Musselman [6] had been adduced against the value of massive dosage, but other laboratory work [7] had encouraged his group to find out what penicillin could do against syphilis when given in massive dosage. Dosage was such as obviated hospitalization and serious interference with the patient's daily work. They had obtained equally good results with two such courses, (i) three intramuscular doses of 500,000 units at hourly intervals for five consecutive days, or (ii) two intramuscular doses of 1,000,000 units at hourly intervals, on each of five days. The combined results of these two courses gave 87 to 92% success in twenty-four cases of primary syphilis and 76 to 92% success in fifty secondary cases. The results of the small series may not be as good as might be obtained by other forms of treatment, but they have the great virtue of having been produced by ambulatory treatment. If course (ii) were supplemented with daily injection of say 0·09 gramme neohalarsine or 0·06 gramme mapharside given in the hour between the two penicillin injections, results might be obtained as good as by any other method but involving far smaller demands on the patients' time and convenience.

He concluded by paying a tribute to the truly remarkable organization, scope and achievement of the American effort, so largely guided and inspired by Dr. Earle Moore.

REFERENCES

1 Liverpool School of Tropical Medicine, 44th Annual Report, August 1, 1942 – July 31, 1943, p. 9.

2 LOURIE, E. M., and COLLIER, H. O. J. (1943) *Ann. trop. Med. Parasit.*, 37, 200.

3 MAHONEY, J. F., ARNOLD, R. C., and HARRIS, A. (1943) *Vener. Dis. Inform.*, 24, 355.

4 ROSS, A. O. F., NELSON, R. B., LOURIE, E. M., COLLIER, H. O. J. (1944) *Lancet* (ii), 845.

5 MOORE, J. E., MAHONEY, J. F., SCHWARTZ, W. H., STERNBERG, T. H., and WOOD, W. B. (1944) *J. Amer. med. Ass.*, 126, 67.

6 EAGLE, H., and MUSSELMAN, A. D. (1944) *J. exp. Med.*, 80, 493.

7 LOURIE, E. M., COLLIER, H. O. J., ROSS, A. O. F., NELSON, R. B., ROBINSON, D. T. (1945) *Lancet* (ii), 696.

Lieut.-Colonel J. W. Eames, R.A.M.C., stated that in 1944 2·4 mega units of penicillin were given in the Army with a failure rate of 8% at the end of six months. Since then further methods have been used but the follow up was difficult. In the case of patients suffering from primary syphilis treated with 2·4 mega units of penicillin (aqueous) over seven and a half days the maximum relapse incidence was in the first six months. The calculated cumulative relapse rate at twelve months for seronegative primary cases was 14% and for seropositive primary cases 13%, and for secondary cases 17·5%. In patients treated with 4 mega units over twelve and a half days, the relapse rate, as far as could be seen from the small follow-up, appeared to be essentially the same. The results of using 2·4 mega units of penicillin plus 0·6 gramme mapharside in ten days, and a similar course giving 0·4 gramme mapharside and 1 gramme bismuth did not appear to differ materially from those obtained by using penicillin alone, but the number followed up had been small. With 2·4 mega units in treatment seroresistance occurred in 3% of seropositive primary cases and 8% of secondary cases and with 4 mega units seropositive primary cases showed a resistance rate of 1·6% and secondary cases 3·8%.

Present treatment in the Army is 50,000 units penicillin three-hourly for ten days, combined with 1·35 grammes N.A.B. and 0·6 gramme bismuth in divided doses on the second, fifth and ninth day followed by 0·6 gramme N.A.B. and 0·2 gramme bismuth weekly for eight weeks. It was too early yet to evaluate this scheme. Bismuth had apparently no effect on the penicillin level of the blood.

Mr. A. J. King felt that now that Dr. Moore had produced the figures it was clear enough there was a considerable failure rate in cases of early syphilis with penicillin alone although such findings did not accord with his own experience. Dr. Curtis and he had limited their inquiries at the Whitechapel Clinic to those discharged soldiers who had received in the Army a total of 2·4 mega units of penicillin in sixty three-hourly injections of 40,000 units each in watery solution. Of 82 patients in this class observed over twelve months at least, in only 4 had treatment failed. This was a very small group and he hoped that other medical officers at other clinics would make similar investigations to obtain a large number of cases observed for a long period.

one is yet prepared to offer any statement as to whether penicillin does cardiovascular syphilis any good, but since it heals visible lesions it should heal lesions which cannot be seen. In contrast to man, however, rabbits with late syphilis appear to be as readily curable with penicillin as do those with early infections. A smaller total dose of penicillin, even, may be required to cure the animals with late than with early syphilis. Is late syphilis in man curable with this drug? Only much further study will give us the information.

In syphilis of the nervous system, regardless of the clinical syndrome present, there are profound and uniform effects from penicillin administered intramuscularly. Whether in asymptomatic neurosyphilis, acute syphilitic meningitis, tabes dorsalis or general paresis, cell count and protein content are reduced to normal in practically all cases. This occurs within a few weeks and in many cases within a few days. Colloidal tests tend towards normal as protein decreases. The spinal fluid Wassermann test is also favourably though more slowly influenced; the rate of reversal of this test depends on the duration of infection with syphilis and the original complement-fixation titre of the fluid. The more strongly positive the fluid the longer it takes for the Wassermann test to become negative. These evidences of laboratory improvement, regardless of the clinical type of the disease, persist at least for three years in about 90% of cases treated: only about 10% of the total showing a later return of fluid abnormalities. There is no need for the technically difficult administration of penicillin by the subdural or intrathecal route. Clinically, penicillin appears to be superior to any form of metal chemotherapy. Regardless of the type of neurosyphilis, clinical improvement may be expected from penicillin to the extent to which symptoms and physical signs depend on inflammation rather than on degeneration. Neither penicillin nor any other form of treatment will restore dead brain cells or fibre tracts, although further destruction and clinical progression may be prevented. In certain of the relatively benign forms of neurosyphilis, penicillin alone gives satisfactory results. In the more serious forms the combination of penicillin and fever from induced malaria may be superior to penicillin alone, both from clinical and laboratory standards. The time-dosage relationship in neurosyphilis is not so clearly established as in early syphilis. Most American observers believe that a large total dose is superior to smaller dosage and that ten to twenty days' treatment is better than a short duration.

The advent of penicillin has made it possible to accomplish as much or more in most cases of neurosyphilis as previously was obtainable with fever and several years of subsequent metal chemotherapy. Its immediate effects appear to be more striking in neurosyphilis than in early syphilis. Available data indicate that penicillin penetrates the tissue of the nervous system in a concentration far lower than that of other tissues. If improvement depends on tissue concentration of the drug, why are results apparently better in neurosyphilis than early syphilis in which the nervous system is spared? Are the good results permanent?

Penicillin represents a major advance in syphilotherapy. There are still a number of curious and unexplained differences in its effect in various stages of syphilitic infection, whether the variable mixtures of commercial penicillin or crystalline penicillin G are used. It probably represents only the first faltering steps in the antibiotic therapy of this disease. Further studies may replace penicillin by a new and more powerful antibiotic. Pending such a development the organized study of penicillin has provided information within four years, which otherwise would have required a generation to accumulate. Further, the co-operative study has re-emphasized the gaps in our knowledge of the fundamental biology of syphilitic infection which must be filled in before the perfect form of treatment of syphilis can be found.

Dr. E. M. Lourie (*Director of the Department of Chemotherapy, Liverpool School of Tropical Medicine*) recalled that his original observations that penicillin was effective against spirochætoses had been made on *Spirochæta recurrentis* and *Spirillum minus* infections in mice in August 1942. Although no secret had been made of the work and its potential significance for syphilis, it did not appear in print until July and December 1943 [1, 2], that is practically simultaneously with the announcement by Mahoney *et al.* [3] that penicillin is, in fact, efficacious against syphilis. Prior to this he had tried unsuccessfully to obtain an allocation for human trials. Detailed plans had already been laid with Dr. A. O. F. Ross for trials against syphilis before Mahoney's paper had appeared, and it was by the merest coincidence that they had chosen a total dosage per case of 2·4 mega units, exactly twice that chosen by the Americans. If penicillin proved to be ineffective at maximal dosages it would then be possible to dismiss the whole subject with relatively little waste of time or penicillin, while, if effective, later effort could be devoted to determining the minimum effective dosage. The results of the first four cases of secondary syphilis he and Dr. Ross treated with 2·4 mega units [4] made them doubt whether penicillin had been as effective as arsenicals and bismuth. The concurrent investigation in the United States [5] of some 1,500 cases of early syphilis

Section of Ophthalmology

President—Harold Levy, F.R.C.S.

[*May* 8, 1947]

CLINICAL MEETING HELD AT THE ROYAL WESTMINSTER OPHTHALMIC HOSPITAL, LONDON

FOUR CASES by A. S. PHILPS, F.R.C.S.

I.—Tuberculous Choroiditis.

A. M., married woman, aged 35. Vision in both eyes has failed for last four months and is now R. 3/60; L. 2/60.

Past history.—One child born eight months ago; followed by mild degree of puerperal sepsis.

Examination.—Cells on the back of both corneæ. and some free cells in the aqueous humour. Lens and vitreous clear. Both fundi show pale masses apparently deep to the retina and most marked around the macular area. The maculæ are both swollen and have deep central pits. No hæmorrhages seen. Appearance resembles that seen in tuberculous choroiditis. No improvement in condition during period under observation.

Mr. P. Moffatt said that in Case I the distribution of the lesions seemed to follow the direction of the vessels to some extent. He wondered whether this condition had started as a phlebitis, possibly of a tuberculous nature.

II.—Retinitis Proliferans.

H. S., married woman, aged 60. Has suffered from diabetes for ten years.

Two years ago.—L. vitreous hæmorrhage, vision reduced to light perception. This hæmorrhage has slowly organized so that at the present time the vitreous contains a number of vascular loops which can be seen growing out from the vessels at the optic disc and forming an almost complete circle.

III.—Palsy of L. Inferior Oblique Muscle.

R. V., aged 34, lorry driver.

Eighteen months ago.—Accident while driving. Crush injury of the face. Depression of the L. maxilla and fracture of the floor of the L. orbit. The depressed fracture was raised by operation shortly after the accident. The history of the muscle palsy and its gradual recovery was shown on the series of Hess charts taken at two-monthly intervals since the accident.

IV.—Asthma, Eczema, Cataract.

P. D., married woman, aged 30.

Skin has always been dry and scaly, sometimes breaking out into a red rash. Asthma started when she was 15 years old, and is so severe that she can never lie flat. Always sleeps with five pillows.

Seven years ago.—The left eye became dim, and subsequently the right.

October 1940: Linear extraction of L. lens. Successful result but later the L. retina detached below.

1947: The R. lens is now quite opaque.

This woman presents the syndrome of asthma, eczema and cataract. Asthma and eczema have often been associated, and dermatogenic cataract has been described by several writers, but the three conditions do not often present themselves in the same patient. The lens being ectodermal in origin, it is not surprising that it develops defects when the skin and epithelium lining the air passages are also affected. The asthma is of such severity that adrenaline injections have frequently to be given and cataract extraction had to be performed with the patient sitting up.

FOUR CASES by P. M. MOFFATT, F.R.C.S.

I.—Intra-ocular Foreign Body. Non-magnetic.

The President said that the intra-ocular foreign body seemed to be definitely metallic, not wood or glass, and his own feeling was that a metallic foreign body inside the eye should be removed. If it was left in, there was invariably degeneration of the retina, and it did not have to be iron or copper to cause that.

Dr. R. Forgan asked whether aqueous penicillin had been given up to 4·8 mega units as had the oil–beeswax suspension and whether there was any indication of a different penicillin optimum for Negroes as compared with whites. Further, were the latest results with crystalline penicillin G so good that an infected American doctor would dare to dispense altogether with metallotherapy?

Dr. David Nabarro stressed Dr. Earle Moore's extraordinarily interesting results in the antenatal treatment of the pregnant mother. When such a drug as penicillin was available it was criminal that positive pregnant mothers should not be treated. The mother need not be treated with a toxic drug but the child would be saved by the use of penicillin. Why children with congenital syphilis responded more readily than adults he could not say. While penicillin would not cure all syphilis, could it so modify the disease that congenital syphilis might appear in unexpected places?

Dr. J. Earle Moore, in reply, said, with reference to Dr. Lourie's series, that one of the things which had been learned and of which he was convinced, was that little or nothing could be said about the results of a small series of patients from any individual clinic. Working with some thirty-five to forty different clinics he had found that clinics using identical treatment schemes had turned up with widely variable results.

In reply to the question "What would you do if you got syphilis?" he would use an ambulatory treatment with penicillin oil–beeswax suspension, mapharside and bismuth.

As regards the use of more than 2·4 million units in aqueous solution, there had been a number of schemes using 4·8 million units and a few with 9·6 million units. With the higher doses there was a suggestion that the results were not quite so good but the differences were not yet statistically significant. With regard to Negroes the point was as to the duration of infection, the negro male being notoriously inaccurate as to the date of his last exposure to infection.

With regard to Dr. Nabarro's remarks he added that in women with primary and secondary syphilis the morbidity and mortality in infants, if the mothers were untreated, was 95%: if the mothers were treated with penicillin it was reduced to somewhere between 1 and 2%. For this one state of syphilitic infection, at any rate, all other methods of treatment should be abandoned and complete reliance placed on penicillin administered to pregnant women. The results were equally good when the mothers were treated late.

A full report of this meeting will appear in the *British Journal of Venereal Diseases.*

Section of Ophthalmology

President—HAROLD LEVY, F.R.C.S.

[*May* 8, 1947]

CLINICAL MEETING HELD AT THE ROYAL WESTMINSTER OPHTHALMIC HOSPITAL, LONDON

FOUR CASES by A. S. PHILPS, F.R.C.S.

I.—Tuberculous Choroiditis.

A. M., married woman, aged 35. Vision in both eyes has failed for last four months and is now R. 3/60; L. 2/60.

Past history.—One child born eight months ago; followed by mild degree of puerperal sepsis.

Examination.—Cells on the back of both corneæ, and some free cells in the aqueous humour. Lens and vitreous clear. Both fundi show pale masses apparently deep to the retina and most marked around the macular area. The maculæ are both swollen and have deep central pits. No hæmorrhages seen. Appearance resembles that seen in tuberculous choroiditis. No improvement in condition during period under observation.

Mr. P. Moffatt said that in Case I the distribution of the lesions seemed to follow the direction of the vessels to some extent. He wondered whether this condition had started as a phlebitis, possibly of a tuberculous nature.

II.—Retinitis Proliferans.

H. S., married woman, aged 60. Has suffered from diabetes for ten years.

Two years ago.—L. vitreous hæmorrhage, vision reduced to light perception. This hæmorrhage has slowly organized so that at the present time the vitreous contains a number of vascular loops which can be seen growing out from the vessels at the optic disc and forming an almost complete circle.

III.—Palsy of L. Inferior Oblique Muscle.

R. V., aged 34, lorry driver.

Eighteen months ago.—Accident while driving. Crush injury of the face. Depression of the L. maxilla and fracture of the floor of the L. orbit. The depressed fracture was raised by operation shortly after the accident. The history of the muscle palsy and its gradual recovery was shown on the series of Hess charts taken at two-monthly intervals since the accident.

IV.—Asthma, Eczema, Cataract.

P. D., married woman, aged 30.

Skin has always been dry and scaly, sometimes breaking out into a red rash. Asthma started when she was 15 years old, and is so severe that she can never lie flat. Always sleeps with five pillows.

Seven years ago.—The left eye became dim, and subsequently the right.

October 1940: Linear extraction of L. lens. Successful result but later the L. retina detached below.

1947: The R. lens is now quite opaque.

This woman presents the syndrome of asthma, eczema and cataract. Asthma and eczema have often been associated, and dermatogenic cataract has been described by several writers, but the three conditions do not often present themselves in the same patient. The lens being ectodermal in origin, it is not surprising that it develops defects when the skin and epithelium lining the air passages are also affected. The asthma is of such severity that adrenaline injections have frequently to be given and cataract extraction had to be performed with the patient sitting up.

FOUR CASES by P. M. MOFFATT, F.R.C.S.

I.—Intra-ocular Foreign Body. Non-magnetic.

The President said that the intra-ocular foreign body seemed to be definitely metallic, not wood or glass, and his own feeling was that a metallic foreign body inside the eye should be removed. If it was left in, there was invariably degeneration of the retina, and it did not have to be iron or copper to cause that.

II.—Familial Macular Degeneration, Adolescent Type.

C. S., male, aged 18, clerk, attended on account of inability to see in the distance. He had been tested many times but was not helped.

R. and L. vision with correction for a small amount of simple myopic astigmatism is 6/60. The fundi show degenerative changes at both maculæ.

He is a Cypriot and has one brother and one sister similarly affected.

III.—Hole at the Macula following Trauma.

IV.—Intra-ocular Secondary Neoplasm.

C. T., aged 58, financier, noticed blurred vision and a dark curtain coming down over the left eye in January 1947. He had been receiving deep X-ray treatment to the left side of the neck in the submaxillary region on account of a mixed salivary tumour which had undergone malignant change.

The retina is now completely detached and can be seen by slit-lamp lying close behind the lens. It shows numerous nodular opacities but no vessels can be traced into them. The intra-ocular tension is raised. Within the last few days some engorged vessels have appeared in the nasal and temporal conjunctiva.

There is a small hard movable nodule in the mid-line of the neck and another in the preauricular region on the right side.

In reply to Mr. Davenport, who asked with regard to Case IV what the retina looked like when first seen, Mr. Moffatt said that it looked like a simple detachment. He examined it by transillumination, and it did transilluminate as far as he could tell. The man had agreed to have the eye excised, and they would then discover what it was.

TWO CASES by M. L. HINE, F.R.C.S.

I.—Retinitis Proliferans.

Male, aged 23.

Loss of vision left eye November 1946. Spots in front of right eye January 1947. All investigations negative.

Left eye: Organizing vitreous hæmorrhage.

Right eye: A few retinal hæmorrhages, with new vessels coming forward into vitreous from an organized hæmorrhage above and out from macula; many retinal bands. Vision is, rather unexpectedly, 6/6.

Diagnosis.—Eales' disease.

II.—? Coats's Disease.

Male, aged 18.

Showed large patches of exudative retinitis, with little pigmentation, mainly external to central area. Some failure of vision commenced in February 1947.

FOUR CASES by T. KEITH LYLE, M.D., M.Chir.

I.—Thrombophlebitis Retinæ.

E. S., female, aged 38.

History.—First attended Royal Westminster Ophthalmic Hospital on February 21, 1947, complaining of sudden loss of vision in the left eye five weeks previously. She noticed this loss first thing in the morning. No improvement had taken place in the meanwhile.

Her vision was 6/6 in the right eye and 3/60 in the left eye. The fundus of the right eye showed some tortuosity of the vessels, particularly below. In the left eye there was œdema of the upper part of the disc, several circular hæmorrhages near the disc and the macular area and the vessels were rather congested.

Her fields showed a large central scotoma in the left eye and constriction of the peripheral field. Fixation was too poor to be accurate. Right eye field was normal. Her W.R. was negative.

Progress.—Very little change has occurred though the hæmorrhage showed a tendency to absorb. A large subhyaloid hæmorrhage was noticed on April 1.

II.—Relative Palsy of Left Superior Rectus Due to Local Orbital Trauma.

E. H., male, aged 32, hairdresser.

Severe head injury whilst on active service in Italy, in July 1945, since when he has suffered from vertical diplopia when looking upwards. No diplopia when looking downwards. Diplopia now becoming worse, but manages to do his job.

Clinical and X-ray examination showed signs of old fracture of left superior maxilla, with resulting enophthalmos and downward displacement of the left eyeball.

There was vertical diplopia when looking upwards a few degrees above the mid-plane. Maximum vertical separation of the images on lævo-elevation, with defective lævo-elevation of left eye. Vision 6/6 each eye. The Maddox rod test (at 6 metres) showed R/L 25^{Δ}; and Eso. 6^{Δ}. Fusion was obtained at $+5^{\Delta}$ with R/L 12^{Δ} on the synoptophore. (Charts were shown of the Hess screen test, the field of binocular single vision and the Maddox rod test at one metre.)

Operation was performed on April 14, 1947. Resection (5 mm.) of the left superior rectus. The result was that all diplopia disappeared and the Maddox rod test (at 6 metres) showed orthophoria. (Charts were shown of post-operative Hess screen test, &c.)

III.—Congenital Palsy of Right Superior Oblique with Compensatory Head Posture (Ocular Torticollis).

A. B., male, aged 38, engineer.

Remembers that his parents noticed he held his head at a peculiar angle. At age of 5 was taken to see Dr. Maddox of Bournemouth who advised an operation (but the advice was not taken!). Prismatic glasses were prescribed instead which he had worn (with periodic alteration in their strength) ever since, but in spite of the glasses he has noticed an increasing tendency to see double (vertical type), which he can sometimes overcome by "cutting out" the vision of the left eye.

He adopts the head posture typical of a case of right superior oblique palsy, i.e. chin depressed, head turned and tilted to left. He has diplopia of the vertical type with maximum vertical separation of images on lævo-depression.

There is defective lævo-depression of right eye, and gross upshoot of right eye on lævoversion. Vision 6/6 each eye. The Maddox rod test (at 6 metres) shows R/L 15^{Δ} with excyclophoria 14°. Fusion was obtained on the synoptophore at 0 with R/L 4^{Δ} but there was no fusional duction power. (The Hess screen chart was shown.)

Operation was performed on December 10, 1946—right inferior oblique myectomy. This was followed by orthoptic treatment.

The diplopia disappeared and the Maddox rod test (at 6 metres) was R/L 1^{Δ} with no cyclophoria. (The post-operative Hess screen chart was shown.) As a result of the orthoptic treatment a full range of fusional duction power was restored.

IV.—Right Superior Oblique Paralysis Due to Right Fourth Cerebral Nerve Palsy Caused by Head Injury.

C. R., male, aged 26, house decorator.

Road accident October 1944. Was unconscious for 9 days. Constant vertical diplopia since the accident.

In spite of two operations performed elsewhere, i.e. (*a*) left inferior rectus recession, (*b*) right inferior oblique myectomy, he still saw double the whole time.

There was vertical diplopia with maximum vertical separation of the images on lævo-depression. He could overcome the diplopia for a short period of time by turning his head to the left, depressing his chin, and tilting his head to left.

There was defective lævo-depression of right eye. The Maddox rod test (at 6 metres) showed R/L 20^{Δ} to 24^{Δ}. Vision was 6/6 each eye. (Charts were shown of the Hess screen test, the field of binocular single vision and the Maddox rod test at one metre.) Fusion was obtained at R/L 4^{Δ} on the synoptophore. Fusional duction power was defective.

Operation was performed on April 1, 1947—re-recession of left inferior rectus (4 mm.). The diplopia disappeared. The Maddox rod test (at 6 metres) was R/L 1^{Δ}, and after a short course of orthoptic treatment full fusional duction power was restored. (Charts were shown of the post-operative Hess screen test.)

THREE CASES by G. G. PENMAN, F.R.C.S.

I.—Choroidal Neoplasm.

A. B., male, aged 34.

History.—First attended Royal Westminster Ophthalmic Hospital on October 21, 1946, complaining of being unable to see clearly for six months with his right eye.

His vision on examination was 6/5 with glasses with each eye. The right fundus showed a pigmented raised area below and temporal to the macula. His field showed a scotoma to red and green corresponding to this appearance.

There has been no change in his condition since, except that on the last occasion he did not read 6/5 as accurately as usual.

II.—Eales' Disease.

II.—Familial Macular Degeneration, Adolescent Type.

C. S., male, aged 18, clerk, attended on account of inability to see in the distance. He had been tested many times but was not helped.

R. and L. vision with correction for a small amount of simple myopic astigmatism is 6/60. The fundi show degenerative changes at both maculæ.

He is a Cypriot and has one brother and one sister similarly affected.

III.—Hole at the Macula following Trauma.

IV.—Intra-ocular Secondary Neoplasm.

C. T., aged 58, financier, noticed blurred vision and a dark curtain coming down over the left eye in January 1947. He had been receiving deep X-ray treatment to the left side of the neck in the submaxillary region on account of a mixed salivary tumour which had undergone malignant change.

The retina is now completely detached and can be seen by slit-lamp lying close behind the lens. It shows numerous nodular opacities but no vessels can be traced into them. The intra-ocular tension is raised. Within the last few days some engorged vessels have appeared in the nasal and temporal conjunctiva.

There is a small hard movable nodule in the mid-line of the neck and another in the pre-auricular region on the right side.

In reply to Mr. Davenport, who asked with regard to Case IV what the retina looked like when first seen, Mr. Moffatt said that it looked like a simple detachment. He examined it by trans-illumination, and it did transilluminate as far as he could tell. The man had agreed to have the eye excised, and they would then discover what it was.

TWO CASES by M. L. HINE, F.R.C.S.

I.—Retinitis Proliferans.

Male, aged 23.

Loss of vision left eye November 1946. Spots in front of right eye January 1947. All investigations negative.

Left eye: Organizing vitreous hæmorrhage.

Right eye: A few retinal hæmorrhages, with new vessels coming forward into vitreous from an organized hæmorrhage above and out from macula; many retinal bands. Vision is, rather unexpectedly, 6/6.

Diagnosis.—Eales' disease.

II.—? Coats's Disease.

Male, aged 18.

Showed large patches of exudative retinitis, with little pigmentation, mainly external to central area. Some failure of vision commenced in February 1947.

FOUR CASES by T. KEITH LYLE, M.D., M.Chir.

I.—Thrombophlebitis Retinæ.

E. S., female, aged 38.

History.—First attended Royal Westminster Ophthalmic Hospital on February 21, 1947, complaining of sudden loss of vision in the left eye five weeks previously. She noticed this loss first thing in the morning. No improvement had taken place in the meanwhile.

Her vision was 6/6 in the right eye and 3/60 in the left eye. The fundus of the right eye showed some tortuosity of the vessels, particularly below. In the left eye there was œdema of the upper part of the disc, several circular hæmorrhages near the disc and the macular area and the vessels were rather congested.

Her fields showed a large central scotoma in the left eye and constriction of the peripheral field. Fixation was too poor to be accurate. Right eye field was normal. Her W.R. was negative.

Progress.—Very little change has occurred though the hæmorrhage showed a tendency to absorb. A large subhyaloid hæmorrhage was noticed on April 1.

II.—Relative Palsy of Left Superior Rectus Due to Local Orbital Trauma.

E. H., male, aged 32, hairdresser.

Severe head injury whilst on active service in Italy, in July 1945, since when he has suffered from vertical diplopia when looking upwards. No diplopia when looking downwards. Diplopia now becoming worse, but manages to do his job.

Clinical and X-ray examination showed signs of old fracture of left superior maxilla, with resulting enophthalmos and downward displacement of the left eyeball.

There was vertical diplopia when looking upwards a few degrees above the mid-plane. Maximum vertical separation of the images on lævo-elevation, with defective lævo-elevation of left eye. Vision 6/6 each eye. The Maddox rod test (at 6 metres) showed R/L 25$^{\Delta}$; and Eso. 6$^{\Delta}$. Fusion was obtained at +5$^{\Delta}$ with R/L 12$^{\Delta}$ on the synoptophore. (Charts were shown of the Hess screen test, the field of binocular single vision and the Maddox rod test at one metre.)

Operation was performed on April 14, 1947. Resection (5 mm.) of the left superior rectus. The result was that all diplopia disappeared and the Maddox rod test (at 6 metres) showed orthophoria. (Charts were shown of post-operative Hess screen test, &c.)

III.—Congenital Palsy of Right Superior Oblique with Compensatory Head Posture (Ocular Torticollis).

A. B., male, aged 38, engineer.

Remembers that his parents noticed he held his head at a peculiar angle. At age of 5 was taken to see Dr. Maddox of Bournemouth who advised an operation (but the advice was not taken!). Prismatic glasses were prescribed instead which he had worn (with periodic alteration in their strength) ever since, but in spite of the glasses he has noticed an increasing tendency to see double (vertical type), which he can sometimes overcome by "cutting out" the vision of the left eye.

He adopts the head posture typical of a case of right superior oblique palsy, i.e. chin depressed, head turned and tilted to left. He has diplopia of the vertical type with maximum vertical separation of images on lævo-depression.

There is defective lævo-depression of right eye, and gross upshoot of right eye on lævoversion. Vision 6/6 each eye. The Maddox rod test (at 6 metres) shows R/L 15$^{\Delta}$ with excyclophoria 14°. Fusion was obtained on the synoptophore at 0 with R/L 4$^{\Delta}$ but there was no fusional duction power. (The Hess screen chart was shown.)

Operation was performed on December 10, 1946—right inferior oblique myectomy. This was followed by orthoptic treatment.

The diplopia disappeared and the Maddox rod test (at 6 metres) was R/L 1$^{\Delta}$ with no cyclophoria. (The post-operative Hess screen chart was shown.) As a result of the orthoptic treatment a full range of fusional duction power was restored.

IV.—Right Superior Oblique Paralysis Due to Right Fourth Cerebral Nerve Palsy Caused by Head Injury.

C. R., male, aged 26, house decorator.

Road accident October 1944. Was unconscious for 9 days. Constant vertical diplopia since the accident.

In spite of two operations performed elsewhere, i.e. (*a*) left inferior rectus recession, (*b*) right inferior oblique myectomy, he still saw double the whole time.

There was vertical diplopia with maximum vertical separation of the images on lævo-depression. He could overcome the diplopia for a short period of time by turning his head to the left, depressing his chin, and tilting his head to left.

There was defective lævo-depression of right eye. The Maddox rod test (at 6 metres) showed R/L 20$^{\Delta}$ to 24$^{\Delta}$. Vision was 6/6 each eye. (Charts were shown of the Hess screen test, the field of binocular single vision and the Maddox rod test at one metre.) Fusion was obtained at R/L 4$^{\Delta}$ on the synoptophore. Fusional duction power was defective.

Operation was performed on April 1, 1947—re-recession of left inferior rectus (4 mm.). The diplopia disappeared. The Maddox rod test (at 6 metres) was R/L 1$^{\Delta}$, and after a short course of orthoptic treatment full fusional duction power was restored. (Charts were shown of the post-operative Hess screen test.)

THREE CASES by G. G. PENMAN, F.R.C.S.

I.—Choroidal Neoplasm.

A. B., male, aged 34.

History.—First attended Royal Westminster Ophthalmic Hospital on October 21, 1946, complaining of being unable to see clearly for six months with his right eye.

His vision on examination was 6/5 with glasses with each eye. The right fundus showed a pigmented raised area below and temporal to the macula. His field showed a scotoma to red and green corresponding to this appearance.

There has been no change in his condition since, except that on the last occasion he did not read 6/5 as accurately as usual.

II.—Eales' Disease.

III.—Dermoid Cyst, Simulating Neoplasm of Lacrimal Gland.

Mrs. J. S., aged 26.

History.—Two years ago a lump in the left upper lid near the outer canthus was incised by her own doctor as ? meibomian cyst. In spite of this, it continued to grow. She was sent to me four months ago. There was then a well-marked ridge in the upper lid, and on everting the lid this ridge was found to be caused by an enlarged lacrimal gland. A small piece of the gland was excised and sectioned, and found to be normal lacrimal tissue. On the assumption that a neoplasm was present deep in the gland, operation was undertaken for its removal. In the gland and deep to it was found a dermoid cyst, with ramifications adherent in one place to the roof of the orbit and in another to its outer wall.

Pathological report.—Dermoid cyst with adjacent normal lacrimal gland.

Cyst is lined partly by keratinized, stratified squamous epithelium, partly by epithelium two or three cells thick, with no keratinization. Contents are amorphous debris with some hairs. In subepithelial tissue are many hair follicles and sebaceous glands, and some inflammatory round cells. A few pieces of cartilage are seen.

A dense fibrous capsule, which has undergone hyaline degeneration, surrounds the cyst, and embedded in this are islands of degenerate striped muscle.

Mr. Eugene Wolff said that he saw the operation done by Mr. Penman on Case III, and the condition was remarkable. He had never seen a dermoid cyst producing that amount of inflammation.

FOUR CASES by EUGENE WOLFF, F.R.C.S.

I.—Lymphoma. ? Diagnosis.

A. B., male, aged 45.

History.—This patient first attended here in 1938 when he was given glasses to correct astigmatism. His vision was 6/5 in each eye. He attended from time to time after that for alteration to his glasses and in August 1946 a small red area appeared just above the upper limbus of the left eye.

Diagnosis was made of episcleritis. He was treated with dionin drops 2% and mist. soda sal. but no relief occurred, in fact the area increased in size.

He was admitted on March 17, 1947, when this area was seen to consist of a mass on the sclera and under the conjunctiva, extending as far forward as the cornea but not actually involving the corneal issue. Biopsy was done and it was noted that the sclera was clean and that the mass was not attached to it.

Investigation.—W.R. negative. Gonococcal fixation test negative; X-ray teeth negative, general physical examination also negative. Microscopic examination of a section showed that the mass consisted of small round cells. It was impossible to say whether it was inflammatory or neoplastic. Further sections are being examined.

Mr. M. L. Hine asked whether if Mr. Wolff regarded Case I as a lymphoma he had considered trying very weak doses of X-rays. In a case which he himself had reported of a woman who had a tumour in the orbit which had been present for a long time, and which was reported on biopsy to be a lymphoma, quite small doses of, he thought, deep X-rays were given in the orbit, and the tumour disappeared as if by magic. The doctor in charge of the department reported that it was an extremely radiosensitive tumour. It was the kind of case which was the dream of the radiologist.

The President said that he remembered once seeing a case of this sort, covering a much larger area than the one now shown, and appearing as something like a sausage across the top of the sclera. It was reported to be a lymphosarcoma. It was a kind of exaggerated edition of the case shown that day and had the same deep colour.

II.—Dermo-Lipoma.

III.—Detached Retina. ? Treatment.

Mr. R. C. Davenport, speaking on Case III of detached retina following injury, said that he saw the case shortly after the injury which was a very severe one. The vitreous was then full of hæmorrhage. That was two years ago. Later the eye showed a lower temporal detachment: the retina was no more detached now and in his opinion was better left alone.

IV.—Result of Blaskowicz Operation for Congenital Ptosis.

Peripheral Cystic Degeneration. ? Prognosis.—J. G. MILNER, F.R.C.S.

L. R., female, aged 45.

History.—For three weeks she had seen a black speck in front of the left eye.

On examination.—Examination showed this was a vitreous opacity in a myopic eye.

Her vision with: $\dfrac{-\ 10\ \text{sph}}{-\ 4{\cdot}5\ \text{cyl. at}\ 20}$: 6/9 Rt. $\dfrac{-\ 10\ \text{sph}}{-\ 4\ \text{cyl. at}\ 160}$: 6/9 Lt.

Both fundi showed inactive peripheral choroiditis in multiple patches. In the upper temporal periphery of the right fundus there was a honeycomb reticulated appearance akin to peripheral cystic degeneration. The problem was whether this area was of great prognostic importance.

Bilateral Coloboma of the Optic Disc.—H. L. Hughes, M.B., B.S., D.O.M.S., (introduced by Professor Arnold Sorsby, F.R.C.S.).

Bilateral coloboma of the optic disc more marked in the right than in the left. In both eyes the coloboma involves mainly the lower part of the disc.

Vision.—Right eye P.L. only. Left eye 6/6.

Refraction under homatropine and cocaine:

$$\text{R.}\quad \begin{array}{c|c} \multicolumn{2}{c}{-5{\cdot}0} \\ \hline & \end{array}\ -4{\cdot}5 \qquad \text{L.}\quad \begin{array}{c|c} \multicolumn{2}{c}{+1{\cdot}25} \\ \hline & \end{array}\ +1{\cdot}25$$

R. Not improved with lenses: L. $\dfrac{+\,0{\cdot}5}{+\,0{\cdot}25 \text{ at 90 degrees}} = 6/5$

Right eye divergent (angle = 40 degrees)

A Family Showing Arachnodactyly with Colobomata of Lenses and Choroid.—R. C. Davenport, F.R.C.S.

The grandmother, deceased, was a patient at Moorfields and had such bad vision that she was nine years at a blind school. She had very long hands and feet (wore size 8 shoes). Nil else known in family.

The mother, aged 33, highly myopic, has worn glasses since childhood and has good vision with them.

Flattened lower edge to each lens, and by slit-lamp section a typical rounded lower border and defective zonule. No displacement of lens. Remnants of fœtal vascular system on lens and in vitreous, particularly in right eye. Fundi appear normal.
Arachnodactylic hands and feet (size 6 in shoes).

The daughter, aged 13. 6/5 vision each eye. Eyes apparently normal, except for defect along line of choroidal cleft in lower right fundus periphery. Hands and feet long, but perhaps not beyond normal.

The son, aged 9. High mixed astigmatism, but sees well with glasses. Like his mother has flattened lower edge of each lens and, like her, no ectopia lentis, but with none of the vestigial vascular remnants. Fundi appear normal. Hands and feet longer than sister's.

Toxoplasmosis: Two Cases.—Professor A. Franceschetti.

Professor A. Franceschetti showed the fundus pictures of two new cases of toxoplasmosis seen in Geneva. They presented coloboma-like destructive lesions of the macular region and some peripheral foci of chorioretinitis. Furthermore there were some sequelæ of a more or less generalized encephalitis. He showed the microscopical section illustrating the first case of toxoplasmosis diagnosed on the Continent by F. Bamatter in Geneva. The mulberry-like aspect of the toxoplasmosis could be demonstrated in the cerebral substance as well as in the retina. Other cases of this kind had been lately discovered in Holland and in Switzerland.

Sir Stewart Duke-Elder said that this was extremely interesting. He had never himself seen a case of toxoplasmosis, and as far as he knew none had been published in this country. The diagnosis ophthalmologically depended upon a coloboma-like destructive lesion of the macula. Was the eye condition necessarily connected with encephalitis elsewhere or could the macula lesion be a condition by itself?

Professor Franceschetti said that in one case not much cerebral alteration was found, but there were symptoms of hypertension. Intracerebral calcification was not seen in all cases. He thought it possible to find certain lesions which, with the ophthalmological symptoms, established the diagnosis.

Asked whether cases terminated fatally, he said that one case had gone on for seven years and another for six, and mentally the patients were able to carry on.

Sir Stewart Duke-Elder said that he thought it quite possible that these cases were occurring and were being missed.

[*June 12, 1947*]

DISCUSSION ON ILLUMINATION

Mr. J. G. Drummond Currie: The subject of artificial illumination is one which is filled with difficulties and interest for ophthalmologists. There is the provision of adequate light, of a right type, in the right place; and there is the fact that all known commercial forms of light are accompanied by a relatively large dissipation of heat. This, in its train, brings in the question of ventilation. Few workers agree upon what is, or is not, a comfortable light in which to work. As ophthalmologists it is so easy for us to be satisfied with our provision of spectacles, when to a large extent we will be ignorant of the conditions under which our prescription will be used. To those who have never had the opportunity of seeing workers at their tasks, I would suggest many visits to factories, not forgetting that the large modern scientifically designed and lighted establishments are by no means typical of the working and lighting conditions under which many people labour. The Factory Lighting Act lays down certain standards, but there is a vast field of offices, &c., not covered by this, and in many cases little count is taken of the decrease in efficiency or strain on the personnel which results from inadequate or badly placed illumination.

There are in general use three main sources of light: The metal filament lamp, the mercury vapour or sodium lamp, and the latest fluorescent tube. Of the three, the metal filament is cheap in first cost, small in bulk, and fairly efficient provided that the fitments are properly placed, adequate in number and of sufficient candle power. But these are fairly high dissipators of heat, poor for colour matching unless proper "correcting" methods are used. The mercury or sodium lamp costs more to install, is cheaper to run, but the wave bands emitted cover a very limited range and therefore coloured objects lose much of their original value. On the other hand the fluorescent tube has all the merits of the mercury or sodium lamp plus a very fair colour rendering and heat losses are relatively small. Stroboscope defects are much more marked in any lamp functioning on the gas discharge principle because, there being no hot filament to cool between the peaks of the cycles, the response to alternating current is almost instantaneous, and, of necessity, a rapid flicker is present all the time. It is true that this fluctuation is not visible under ordinary conditions, but it can make movement in machinery at certain speeds give the deceptive effect of being stationary or produce the rather unpleasant effect of a jerky movement. This stroboscope effect can be minimized by such devices as installing the lights in "staggered" phase, but it is still present, and one wonders if one day a combination of fluorescent materials with those of the phosphorescent group may not give continuous light. Fear by the workers that harmful ultraviolet rays may be emitted by these new lamps is, I think, groundless. By the time the existing wavelength of ultraviolet has stimulated the fluorescent material and passed through the glass, no more radiation takes place than occurs from an ordinary metal filament bulb.

I would suggest a few short rules to be borne in mind: First, that light should be adequate for the type of work, and the source chosen should be of a suitable type both as regards lamp and fitting, not forgetting colour rendering. Secondly, that it should be installed in such a position that the source of light is not too near the direct line of vision. Thirdly, that shadows should be avoided as much as possible, with the exception of those types of "operation" where unidirectional light is desirable. Fourthly, that specular reflection and too much heat are great disadvantages. Lastly, that too great a contrast of surrounding objects can be tiring and even dangerous. And in this last category do not forget the beneficial effect of reflection from properly decorated walls and ceilings.

Dr. J. W. T. Walsh (*National Physical Laboratory*): *Brightness and illumination.*—It has sometimes been said that the illuminating engineer should more properly regard himself as a brightness engineer since what the eye appreciates is brightness and not illumination. On the other hand the engineer is in two difficulties if he tries to design for brightness. In the first place the brightness of an object, measured by a photometer, depends partly on the illumination and partly on the reflection characteristics of the object, and the latter are usually quite out of the illuminating engineer's control. Even worse than this is the fact that the photometer does not tell the whole story. The word "brightness", as it is commonly used, may mean either of two things which are related but not uniquely. The word as used by the engineer generally denotes the quantity which the photometer measures, the physical attribute of an illuminated object. The same word is, however, at least as commonly used to denote one attribute of the sensation produced when an object is looked at, viz. that attribute by means of which objects may be arranged in a series of increasing or decreasing brightness. It is necessary to draw a clear distinction between these two meanings and to qualify the word by an adjective which shows clearly which meaning is intended. For the engineering or physical meaning the term "photometric brightness" may be used, the term "subjective brightness" being employed whenever the sensation is meant.

Illumination.—The photometric brightness of any given surface is proportional to its illumination, i.e. to the amount of luminous flux it receives per unit area. For a long time the notion of illumination was derived from that of luminous intensity, or candle-power. A surface was imagined to be placed at a known distance from a source of light of known candle-power and the illumination of the surface, if perpendicular to the light rays, was said to be equal to I/d^2 when I was the candle-power of the source in the direction of the surface and d the distance of the surface from the source. If d was measured in feet and I in candles, I/d^2 was expressed in foot-candles. Of course if the surface was inclined at an angle θ from perpendicularity to the light, the illumination was reduced to the value $(I/d^2) \cos \theta$ foot-candles.

This method of deriving the expression for illumination and the unit in which it was measured has now been superseded in illuminating engineering and it is customary to regard illumination as the surface density of incident light or, more precisely, of luminous flux. Luminous flux is measured in lumens and to indicate the order of magnitude it may be mentioned that the tungsten lamp (in the sizes used for indoor lighting) gives about 10 lumens per watt, while the new fluorescent tubular lamp gives about 38 lumens per watt (taking the average figure throughout the life of the tube) so that the luminous flux output from an 80 watt lamp is about 3,000 lumens.

Illumination, being the surface density of luminous flux, is measured in lumens per sq. ft. In fact, one lumen per sq. ft. is precisely the same as one foot-candle; they are two names for the same thing and only the method of approach is different.

The objection has been raised that the term "lumens per sq. ft.", although self-explanatory and satisfactory in written form, especially if abbreviated as lm/ft^2, does not lend itself readily to speech and it must be admitted that the full term is cumbersome. Alternative names have been suggested but the whole matter is still *sub judice*. Meanwhile, values of illumination in such documents as the Illuminating Engineering Society's Code of Good Lighting Practice are all now expressed in lumens per square foot, instead of in foot-candles.

Photometric brightness.—The photometric brightness of a surface may be measured and expressed in two ways. Every object can be regarded as a source of light, either primary or secondary. Objects which generate the light they emit are termed primary sources, while all others, which act as sources only in so far as they reflect some of the light they receive from a primary source, are secondary sources. Although the distinction is convenient the fact remains that any object is a light source and as such has a photometric brightness. In the case of a primary source the brightness is usually expressed as the candle-power of the source divided by its apparent area, both measured in the direction of view, e.g. in candles per square inch.

In an exactly similar way, the photometric brightness of any secondary source, such as an illuminated surface, can be expressed by its candle-power per unit area, but as the brightness is usually much lower the unit of area chosen is most often the square foot instead of the square inch.

It will be clear that the relation between the photometric brightness of a surface and its illumination is dependent on that property of the surface which is usually called its reflection factor. This quantity is defined as the fraction of the incident luminous flux which the surface reflects, the remainder being absorbed or transmitted.

Different kinds of surfaces distribute the luminous flux which they reflect in different ways. For matt surfaces the distribution is sufficiently uniform to give the impression that the photometric brightness is the same in all directions, but for every practical purpose the brightness varies with the direction of view. With some surfaces the departures from uniformity are comparatively small and an ideal surface in which the brightness is perfectly uniform is a convenient conception, usually referred to as a perfect diffuser.

The importance of the perfect diffuser is that, since the flux distribution is completely defined by the fact that the brightness is independent of the direction of view, this brightness can be related immediately to the illumination and to the reflection factor. In fact the brightness, in candles per sq. ft., is equal to the illumination in lumens per sq. ft. multiplied by the reflection factor and divided by the constant π.

The intrusion of this constant is often avoided by using a different unit for photometric brightness, a unit which is equal to $1/\pi$ candle per sq. ft. This unit is known as the foot-lambert and it will be seen that the brightness of a perfectly diffusing surface in foot-lamberts is equal to its illumination in lumens per sq. ft. multiplied by its reflection factor. For an ordinary matt surface the relation, although not strictly true, holds sufficiently well for many practical purposes.

[*June* 12, 1947]

DISCUSSION ON ILLUMINATION

Mr. J. G. Drummond Currie: The subject of artificial illumination is one which is filled with difficulties and interest for ophthalmologists. There is the provision of adequate light, of a right type, in the right place; and there is the fact that all known commercial forms of light are accompanied by a relatively large dissipation of heat. This, in its train, brings in the question of ventilation. Few workers agree upon what is, or is not, a comfortable light in which to work. As ophthalmologists it is so easy for us to be satisfied with our provision of spectacles, when to a large extent we will be ignorant of the conditions under which our prescription will be used. To those who have never had the opportunity of seeing workers at their tasks, I would suggest many visits to factories, not forgetting that the large modern scientifically designed and lighted establishments are by no means typical of the working and lighting conditions under which many people labour. The Factory Lighting Act lays down certain standards, but there is a vast field of offices, &c., not covered by this, and in many cases little count is taken of the decrease in efficiency or strain on the personnel which results from inadequate or badly placed illumination.

There are in general use three main sources of light: The metal filament lamp, the mercury vapour or sodium lamp, and the latest fluorescent tube. Of the three, the metal filament is cheap in first cost, small in bulk, and fairly efficient provided that the fitments are properly placed, adequate in number and of sufficient candle power. But these are fairly high dissipators of heat, poor for colour matching unless proper ''correcting' methods are used. The mercury or sodium lamp costs more to install, is cheaper to run, but the wave bands emitted cover a very limited range and therefore coloured objects lose much of their original value. On the other hand the fluorescent tube has all the merits of the mercury or sodium lamp plus a very fair colour rendering and heat losses are relatively small. Stroboscope defects are much more marked in any lamp functioning on the gas discharge principle because, there being no hot filament to cool between the peaks of the cycles, the response to alternating current is almost instantaneous, and, of necessity, a rapid flicker is present all the time. It is true that this fluctuation is not visible under ordinary conditions, but it can make movement in machinery at certain speeds give the deceptive effect of being stationary or produce the rather unpleasant effect of a jerky movement. This stroboscope effect can be minimized by such devices as installing the lights in ''staggered'' phase, but it is still present, and one wonders if one day a combination of fluorescent materials with those of the phosphorescent group may not give continuous light. Fear by the workers that harmful ultraviolet rays may be emitted by these new lamps is, I think, groundless. By the time the existing wavelength of ultraviolet has stimulated the fluorescent material and passed through the glass, no more radiation takes place than occurs from an ordinary metal filament bulb.

I would suggest a few short rules to be borne in mind: First, that light should be adequate for the type of work, and the source chosen should be of a suitable type both as regards lamp and fitting, not forgetting colour rendering. Secondly, that it should be installed in such a position that the source of light is not too near the direct line of vision. Thirdly, that shadows should be avoided as much as possible, with the exception of those types of ''operation'' where unidirectional light is desirable. Fourthly, that specular reflection and too much heat are great disadvantages. Lastly, that too great a contrast of surrounding objects can be tiring and even dangerous. And in this last category do not forget the beneficial effect of reflection from properly decorated walls and ceilings.

Dr. J. W. T. Walsh (*National Physical Laboratory*): *Brightness and illumination.*—It has sometimes been said that the illuminating engineer should more properly regard himself as a brightness engineer since what the eye appreciates is brightness and not illumination. On the other hand the engineer is in two difficulties if he tries to design for brightness. In the first place the brightness of an object, measured by a photometer, depends partly on the illumination and partly on the reflection characteristics of the object, and the latter are usually quite out of the illuminating engineer's control. Even worse than this is the fact that the photometer does not tell the whole story. The word ''brightness'', as it is commonly used, may mean either of two things which are related but not uniquely. The word as used by the engineer generally denotes the quantity which the photometer measures, the physical attribute of an illuminated object. The same word is, however, at least as commonly used to denote one attribute of the sensation produced when an object is looked at, viz. that attribute by means of which objects may be arranged in a series of increasing or decreasing brightness. It is necessary to draw a clear distinction between these two meanings and to qualify the word by an adjective which shows clearly which meaning is enough of it, hence the eyes are required to operate too long at a distance which involves an undue muscular effort for accommodation and convergence.

This statement, which applies to many offices, factories, homes and other places, raises the question, "how much illumination is necessary for the performance of different visual tasks efficiently and without eyestrain?"

There is more than one method of getting an answer to this question. One way is to ascertain what, on the average, is the illumination currently used for different purposes. I need not enumerate the shortcomings of this method: suffice it to say that actual usage at any time is not necessarily determined by the real need of the user and, even in pre-Shinwellian times, there was always a general tendency towards direct economy in artificial lighting. When practice is freely determined, we find people who have really fine work to do choosing very high illuminations : For example, the lace-makers of Bruges and Geneva, who do their work, when they can, out-of-doors, where they often get more than 1,000 lumens per square foot; while most of us prefer to read, write or do other close work, near a window from which, in daytime, we can often get ten or twenty times more light than we put up with from artificial sources at night.

Another way is to determine, experimentally, the level of illumination at which the performance of particular visual tasks comes to a maximum. By this means, the optimum illuminations have been found for some specific occupations, and since the latter are visually comparable with others, it can be inferred that similar illuminations are suitable for these.

A third method consists in analysing the particular objects involved in any given task and appraising them in respect of certain characteristics, whose magnitudes determine the visual capacities required to see the objects easily. The principal characteristics with which we are concerned are the size and distance of the details that need to be distinguished, as well as the reflectivity of these details and of their immediate surrounds. Then—from what is known concerning the way in which visual performance varies with variation of size, contrast and illumination—a value of the latter can be found which will be appropriate for the task considered.

For practical application this method has been simplified, as far as possible, by the preparation of a chart which is included, with suitable explanatory notes, in the Illuminating Engineering Society's Lighting Code.

A point to notice particularly is that illumination values should rise in geometrical or equal ratio steps. The reason for this is that successively larger increments of illumination are necessary to increase visual capacity step by step, just as they are to produce, successively, an apparent difference of brightness. In other words, illumination should be increased in *proportion* to its value at the beginning of each step, rather than by equal increments, which would become progressively less effective; just as an increment of £10 when income is £1,000 would be far less satisfying than it would be when income is only £100.

The proportional increase upon each value to the next above it in the I.E.S. scales is not strictly constant, simply because to make it so would lead to inconvenient fractional values. The average increment, however, is one of nearly 50%, and, in practice, it is difficult to discriminate between visual tasks for which any smaller relative difference of illumination would be appropriate.

In the I.E.S. Code there is also a schedule of values of illumination necessary on the objects of special regard in various Interiors or Occupations. These values have been arrived at by the methods I have mentioned—chiefly, however, by the first and second. They can be accepted with considerable confidence, but are not final, and are subject to revision as and when the need for this becomes apparent.

Three values may be selected to show how widely different are the requirements for different visual tasks. First, in the home, 7 lumens per sq. ft. is recommended on cookers, sinks and tables, where there are specific visual tasks to be done. These involve the perception of detail which, on the whole, is of "ordinary" size, and is in moderate contrast with its background. The recommended value is found on the I.E.S. chart in the B scale—which is applicable to cases of moderate contrast—opposite the division numbered 5 on the size scale.

Secondly, in industry, 30 lumens per sq. ft. is recommended for weaving medium worsted fabrics. Here, the detail involved just comes within the small category and, again, there is only a moderate difference between the reflection factors of detail and ground. Thirdly, in the hospital, 300 lumens per sq. ft. is recommended on operating tables, because the detail to be seen is often very small, and the contrast between the parts the surgeon must distinguish may be very poor, so that the appropriate illumination is to be looked for on the C scale of the Chart.

(Mr. Weston showed a slide illustrating the I.E.S. Illumination Chart.)

It may, perhaps, be regarded as regrettable that there should be two systems of photometric brightness units, but actually they are generally used for different purposes; the brightness of a primary source, such as a fluorescent lamp, is usually expressed in candles per square inch, while the brightness of illuminated surfaces is expressed in foot-lamberts. It may be worth noting that the former unit is, to an accuracy of about 10%, 500 times as large as the latter.

Measurement.—Both illumination and brightness can be measured visually with a special form of portable photometer which contains a comparison surface illuminated by a small battery lamp. The brightness of this surface is varied, by moving the lamp or otherwise, until it matches an external white surface placed at the position at which the illumination is to be measured. A scale attached to the device by which the brightness of the comparison surface is varied gives, by previous calibration, the illumination of the external surface.

In order to measure brightness with this instrument it is necessary to know the ratio of brightness to illumination for the external white surface. This is usually given as the "reflection factor" of the surface, and it will be seen that if this is ρ and the instrument reading when viewing *any* surface is multiplied by ρ the product will be the photometric brightness of the surface in foot-lamberts.

For illumination measurements photo-electric instruments are replacing visual photometers. Light reaching the surface of the photocell is converted into electrical energy and the current generated by the cell is, within certain limitations, proportional to the illumination of the cell. One of the limitations is that the cell does not behave in the same way as the eye to light of different colours, with the result that if the instrument is calibrated for, say, the light given by a tungsten lamp the readings for daylight or for the light given by a fluorescent lamp have to be multiplied by a correction factor. Further, the response of the cell is less when the light is incident obliquely, at any rate for angles of 60 degrees or more with the normal. The familiar photo-electric exposure meter used by the photographer is an example of the application of an instrument of this kind to brightness measurement.

Mr. H. C. Weston (*Medical Research Council*): Dr. Walsh has dealt with the measurement of illumination and brightness, and my remarks will be confined to the illumination requirements of the eye, and to one or two points concerning artificial lighting.

The view is still often expressed that artificial light is not good for the eyes, at any rate if one has to rely upon it for long periods. One of the reasons advanced for this belief is that artificial light differs qualitatively and visibly from natural light. True, the spectral composition of the light given by artificial sources now commonly used is not identical with that of daylight; nor can it be made so, since the latter is subject to diurnal variations of colour quality. Nevertheless, most of these sources give what is broadly called "white" light, and it has never been shown that healthy eyes suffer any harmful effects which can be attributed to the "make-up" of the luminous flux emitted by such sources.

Even in the case of mercury and sodium electric discharge lamps, which have a discontinuous spectrum and emit bluish and yellow light respectively, there is no evidence that this characteristic is responsible for any organic changes which impair the sight. These lamps may be unsuitable for use in some circumstances, because of their colour-rendering properties and of the inconvenience or displeasure this may occasion, but these effects do no harm to the visual system.

The relatively new, but now widely used, fluorescent lighting, although generally very popular, has led to a number of complaints of ill-effects, as well as to some ill-considered speculations concerning the harm it might do. Most of the complaints of which I have personal knowledge have been vaguely expressed, and in these cases there have been no external signs of ocular disturbance. A sensation of strain is usually mentioned, so also is headache. Inquiry has usually elicited the fact that headaches were not uncommonly experienced before exposure to fluorescent lighting. The complaints have come chiefly from persons of psychoneurotic type—as judged by interview and medical history—and most of these people have been found to be working with low illumination. Badly planned installations are certainly responsible for some cases of dissatisfaction, and this is equally true when other types of light source are used.

Fears have been expressed concerning the effects of ultraviolet radiation emitted by fluorescent lamps, but there is none of shorter wavelength than is present in diffuse daylight, and its intensity at ordinary levels of illumination appears to be much less than is believed to be necessary for any abiotic action.

The only other objection to fluorescent lighting which seems to me to be worth discussion is on the score of flicker, as apparent in the so-called stroboscopic effect. There is no doubt that this is more or less disconcerting to some people, but certainly not to the majority. It can be made unobjectionable in multi-lamp installations.

I think there is no doubt that artificial light is not bad for the eyes on account of any qualitative dissimilarity to daylight; but it is very often bad for them because there is not enough of it, hence the eyes are required to operate too long at a distance which involves an undue muscular effort for accommodation and convergence.

This statement, which applies to many offices, factories, homes and other places, raises the question, "how much illumination is necessary for the performance of different visual tasks efficiently and without eyestrain?"

There is more than one method of getting an answer to this question. One way is to ascertain what, on the average, is the illumination currently used for different purposes. I need not enumerate the shortcomings of this method: suffice it to say that actual usage at any time is not necessarily determined by the real need of the user and, even in pre-Shinwellian times, there was always a general tendency towards direct economy in artificial lighting. When practice is freely determined, we find people who have really fine work to do choosing very high illuminations : For example, the lace-makers of Bruges and Geneva, who do their work, when they can, out-of-doors, where they often get more than 1,000 lumens per square foot; while most of us prefer to read, write or do other close work, near a window from which, in daytime, we can often get ten or twenty times more light than we put up with from artificial sources at night.

Another way is to determine, experimentally, the level of illumination at which the performance of particular visual tasks comes to a maximum. By this means, the optimum illuminations have been found for some specific occupations, and since the latter are visually comparable with others, it can be inferred that similar illuminations are suitable for these.

A third method consists in analysing the particular objects involved in any given task and appraising them in respect of certain characteristics, whose magnitudes determine the visual capacities required to see the objects easily. The principal characteristics with which we are concerned are the size and distance of the details that need to be distinguished, as well as the reflectivity of these details and of their immediate surrounds. Then—from what is known concerning the way in which visual performance varies with variation of size, contrast and illumination—a value of the latter can be found which will be appropriate for the task considered.

For practical application this method has been simplified, as far as possible, by the preparation of a chart which is included, with suitable explanatory notes, in the Illuminating Engineering Society's Lighting Code.

A point to notice particularly is that illumination values should rise in geometrical or equal ratio steps. The reason for this is that successively larger increments of illumination are necessary to increase visual capacity step by step, just as they are to produce, successively, an apparent difference of brightness. In other words, illumination should be increased in *proportion* to its value at the beginning of each step, rather than by equal increments, which would become progressively less effective; just as an increment of £10 when income is £1,000 would be far less satisfying than it would be when income is only £100.

The proportional increase upon each value to the next above it in the I.E.S. scales is not strictly constant, simply because to make it so would lead to inconvenient fractional values. The average increment, however, is one of nearly 50%, and, in practice, it is difficult to discriminate between visual tasks for which any smaller relative difference of illumination would be appropriate.

In the I.E.S. Code there is also a schedule of values of illumination necessary on the objects of special regard in various Interiors or Occupations. These values have been arrived at by the methods I have mentioned—chiefly, however, by the first and second. They can be accepted with considerable confidence, but are not final, and are subject to revision as and when the need for this becomes apparent.

Three values may be selected to show how widely different are the requirements for different visual tasks. First, in the home, 7 lumens per sq. ft. is recommended on cookers, sinks and tables, where there are specific visual tasks to be done. These involve the perception of detail which, on the whole, is of "ordinary" size, and is in moderate contrast with its background. The recommended value is found on the I.E.S. chart in the B scale—which is applicable to cases of moderate contrast—opposite the division numbered 5 on the size scale.

Secondly, in industry, 30 lumens per sq. ft. is recommended for weaving medium worsted fabrics. Here, the detail involved just comes within the small category and, again, there is only a moderate difference between the reflection factors of detail and ground. Thirdly, in the hospital, 300 lumens per sq. ft. is recommended on operating tables, because the detail to be seen is often very small, and the contrast between the parts the surgeon must distinguish may be very poor, so that the appropriate illumination is to be looked for on the C scale of the Chart.

(Mr. Weston showed a slide illustrating the I.E.S. Illumination Chart.)

So much for the illumination required on objects to which we must give special attention; but the illumination of the general field of view should be suitably proportioned to that of the restricted field of interest, so that there may be no great difference between the brightness of the latter and that of the panorama. As you know, this has been shown to be a necessary condition for the development of high acuity. It is also desirable to prevent the need for any considerable change of adaptation every time the gaze is shifted from the local field of work, and to avoid the feeling of gloom so generally associated with dark surrounds.

When local areas of the visual field have a brightness greatly exceeding the prevailing general level glare is usually experienced. This happens in rooms having very small windows and dark-coloured walls, but it is more frequently due to artificial lighting, owing to the still common practice of using unsuitable lighting fittings which do not screen the bare lamps from the eyes at all usual angles of view, or do not have a sufficiently low surface brightness.

People who complain of artificial light as being "too bright" generally mean—whether they realize it or not—that the *sources of light* are glaring, and not that there is too much light on the objects it is desired to see.

I need not enlarge upon the undesirable effects of glare, but will only remind you that they are quite frequently caused by the reflection of light from shiny surfaces in the normal field of view, and not only by the direct view of lighting units. When the presence of such surfaces is unavoidable—and they are often the actual objects of work—the lighting installation needs to be carefully planned to prevent images of the actual light sources from being seen in these surfaces.

Providing there is careful design for the avoidance of glare, the highest general illumination which is likely to be provided by artificial lighting in most buildings cannot be harmful to healthy eyes, for it is known that vision continues to improve as illumination rises, at least up to 1,000 lumens per sq. ft.

All the values of illumination given in the I.E.S. Code, and in other Codes of Practice, as well as in the Factory Lighting Regulations, have reference to the needs of average-sighted persons, and their effectiveness is conditional upon the avoidance of glare and the proper direction and diffusion of the light. For sub-sighted persons higher values of illumination are desirable.

In view of the growing proportion of the working population distributed in the older age-groups, the standard of vision that must be taken as the average is becoming lower.

The effect of this upon our industrial productivity may be more serious than might be supposed, unless the standards of illumination are improved, and a more extensive use is made of other aids to vision.

The effect of age upon the amplitude of accommodation of the eye is well known. Advancing age is also accompanied by some loss of visual acuity, some loss of transparency of the media, particularly to blue light, and by a reduction of the mean size of the pupil. It is also well known that partly for these reasons, most people—at any rate from middle-age onwards—become increasingly conscious of the need for good illumination for the performance of common visual tasks.

Surprisingly, however, very little is known concerning the actual relationship between age and the speed and accuracy with which different grades of visual task can be performed, and of the way in which this relationship is modified by varying the illumination of the objects of vision.

Recent experimental evidence—not yet published—shows that visual performance in this sense falls off continuously from an unexpectedly early age, and the rate of decline with age—though it naturally differs according to the severity of the visual task—is not inconsiderable, except with very easy tasks.

For example, if the visual task consists of distinguishing the name of a subscriber printed in the Telephone Directory, it seems likely that year by year, after the age of 21, we shall do it more slowly, and the *annual* loss of speed, between the twenties and the forties, may be as much as 3 or 4%.

[Here Mr. Weston showed a graph plotted from the results of two series of experiments made with small groups of subjects differing in age, who performed a visual task comparable with the practical example mentioned. It showed the continuous decline of visual performance during the middle third of the normal span of life, the annual decrement being of the magnitude suggested.]

If the visual task is made more difficult, either by reducing the size of the objects, or reducing the contrast between them and their background, then the slope of the curve relating performance with age becomes steeper, i.e. the annual loss of visual performance becomes greater. Conversely, with easier visual tasks, the adverse effect of advancing age is less marked.

Because its occurrence is insidious—like the depreciation of the power of accommodation—this loss of visual efficiency is not realized until it has progressed so far as to become a nuisance in daily life, as it does at about the age when it is usual to get a first prescription for so-called presbyopia. But it is probably not a loss which can be ascribed to ocular changes alone. Presumably there is ageing of the extra-ocular central nervous parts of the visual apparatus, and this may account partly for the decline in performance.

The rate of decline can be diminished by improving illumination, although the effect of age cannot be offset entirely by this means. As age advances, a given increment of illumination, say a doubling, is relatively more effective; that is to say, it brings about a greater *percentage* improvement of visual performance, for example, at the age of 45 than it does at the age of 35, and the more so the smaller the objects which have to be seen. Even so, the improvement is not enough to nullify the toll of time. All we can do is to minimize this toll and, if this is to be done, even the under-forties require higher levels of illumination for some everyday visual tasks than are often provided by artificial light.

Two short films made by the General Electric Company of Wembley were then shown, both illustrating the effect of illumination and colour on the ease with which fine work could be executed.

The first showed the threading of a needle, and the second industrial lathe work. They showed especially that the direction of illumination was even more important than the quality and amount.

The President, in opening the discussion, drew attention to a question ophthalmic surgeons were often asked by patients, namely, what was the best light by which to do a certain type of work. He had personally found that a somewhat difficult question to answer.

Mr. F. A. Williamson-Noble said that he would like to obtain a copy of the artificial lighting chart[1] shown on the screen because he, like the President, was constantly bombarded with the question as to the best light a certain piece of work should be done by. His usual answer was to hand to the inquirer the pamphlet on lighting in schools which gave at the end a table showing the amount of light required for various purposes but that was not so comprehensive as the chart shown during the opening remarks.

With regard to the use of glazed paper in books he personally was constantly bothered by the reflection from the paper and often wondered whether the use of glazed paper should be banned from books. A matt surface would be very much better though that might affect the contrast between the printing ink and the background.

Dr. F. W. Sharpley said he was always finding himself up against the question of glare; although a great deal of work had already been done in that regard much more required to be done. He did not think the effect of glare in everyday life was sufficiently realized. He was not referring particularly to such glare as that caused by specular reflection from glazed paper but, more generally, to the effect of direct light from the source of illumination both in the case of artificial illuminants and natural illumination from the sky through windows. He had noticed in practice so many instances in which glare effect could be reduced by very simple means. It was, to some extent, a matter of educating the public. A matter which might be of interest to ophthalmic surgeons was the question of the more extensive use of eyeshades, such as compositors used, for operations for which they were not now used. One might find, for instance, that a typist was typing against the light, which was obviously wrong, but there were instances in which it was difficult to avoid that position. In such cases an eyeshade would be helpful, to mitigate the effects of glare but one seldom saw it used. It would be interesting to hear what ophthalmic surgeons had to say with regard to the more extensive use of eyeshades.

The use of fluorescent lamps was often recommended as a means of reducing glare because there was a larger source and, consequently, a lower surface brightness for a given candle-power. It did not seem to be as fully appreciated as it might be that that lower brightness did reduce the glare in one sense, but there was still an appreciable degree of glare from the disability point of view, just as there was from a large daylight window. One could easily detect the effect of that glare by simply shading the eyes momentarily from the source while observing an object in the same field of view.

With regard to the flicker from fluorescent lamps, the use of lamps on different phases staggered over the factory system was one way of reducing the flicker though it did not altogether abolish the effect, particularly in the peripheral field of view. The speaker did not think a self-contained three-phase lamp had yet been produced, but such a lamp with a

[1] Procurable from the Illuminating Engineering Society, 32, Victoria Street, London, S.W. Included in "I.E.S. Code for the Lighting of Building Interiors." 1s. 6d.

So much for the illumination required on objects to which we must give special attention; but the illumination of the general field of view should be suitably proportioned to that of the restricted field of interest, so that there may be no great difference between the brightness of the latter and that of the panorama. As you know, this has been shown to be a necessary condition for the development of high acuity. It is also desirable to prevent the need for any considerable change of adaptation every time the gaze is shifted from the local field of work, and to avoid the feeling of gloom so generally associated with dark surrounds.

When local areas of the visual field have a brightness greatly exceeding the prevailing general level glare is usually experienced. This happens in rooms having very small windows and dark-coloured walls, but it is more frequently due to artificial lighting, owing to the still common practice of using unsuitable lighting fittings which do not screen the bare lamps from the eyes at all usual angles of view, or do not have a sufficiently low surface brightness.

People who complain of artificial light as being "too bright" generally mean—whether they realize it or not—that the *sources of light* are glaring, and not that there is too much light on the objects it is desired to see.

I need not enlarge upon the undesirable effects of glare, but will only remind you that they are quite frequently caused by the reflection of light from shiny surfaces in the normal field of view, and not only by the direct view of lighting units. When the presence of such surfaces is unavoidable—and they are often the actual objects of work—the lighting installation needs to be carefully planned to prevent images of the actual light sources from being seen in these surfaces.

Providing there is careful design for the avoidance of glare, the highest general illumination which is likely to be provided by artificial lighting in most buildings cannot be harmful to healthy eyes, for it is known that vision continues to improve as illumination rises, at least up to 1,000 lumens per sq. ft.

All the values of illumination given in the I.E.S. Code, and in other Codes of Practice, as well as in the Factory Lighting Regulations, have reference to the needs of average-sighted persons, and their effectiveness is conditional upon the avoidance of glare and the proper direction and diffusion of the light. For sub-sighted persons higher values of illumination are desirable.

In view of the growing proportion of the working population distributed in the older age-groups, the standard of vision that must be taken as the average is becoming lower.

The effect of this upon our industrial productivity may be more serious than might be supposed, unless the standards of illumination are improved, and a more extensive use is made of other aids to vision.

The effect of age upon the amplitude of accommodation of the eye is well known. Advancing age is also accompanied by some loss of visual acuity, some loss of transparency of the media, particularly to blue light, and by a reduction of the mean size of the pupil. It is also well known that partly for these reasons, most people—at any rate from middle-age onwards—become increasingly conscious of the need for good illumination for the performance of common visual tasks.

Surprisingly, however, very little is known concerning the actual relationship between age and the speed and accuracy with which different grades of visual task can be performed, and of the way in which this relationship is modified by varying the illumination of the objects of vision.

Recent experimental evidence—not yet published—shows that visual performance in this sense falls off continuously from an unexpectedly early age, and the rate of decline with age—though it naturally differs according to the severity of the visual task—is not inconsiderable, except with very easy tasks.

For example, if the visual task consists of distinguishing the name of a subscriber printed in the Telephone Directory, it seems likely that year by year, after the age of 21, we shall do it more slowly, and the *annual* loss of speed, between the twenties and the forties, may be as much as 3 or 4%.

[Here Mr. Weston showed a graph plotted from the results of two series of experiments made with small groups of subjects differing in age, who performed a visual task comparable with the practical example mentioned. It showed the continuous decline of visual performance during the middle third of the normal span of life, the annual decrement being of the magnitude suggested.]

If the visual task is made more difficult, either by reducing the size of the objects, or reducing the contrast between them and their background, then the slope of the curve relating performance with age becomes steeper, i.e. the annual loss of visual performance becomes greater. Conversely, with easier visual tasks, the adverse effect of advancing age is less marked.

Because its occurrence is insidious—like the depreciation of the power of accommodation—this loss of visual efficiency is not realized until it has progressed so far as to become a nuisance in daily life, as it does at about the age when it is usual to get a first prescription for so-called presbyopia. But it is probably not a loss which can be ascribed to ocular changes alone. Presumably there is ageing of the extra-ocular central nervous parts of the visual apparatus, and this may account partly for the decline in performance.

The rate of decline can be diminished by improving illumination, although the effect of age cannot be offset entirely by this means. As age advances, a given increment of illumination, say a doubling, is relatively more effective; that is to say, it brings about a greater *percentage* improvement of visual performance, for example, at the age of 45 than it does at the age of 35, and the more so the smaller the objects which have to be seen. Even so, the improvement is not enough to nullify the toll of time. All we can do is to minimize this toll and, if this is to be done, even the under-forties require higher levels of illumination for some everyday visual tasks than are often provided by artificial light.

Two short films made by the General Electric Company of Wembley were then shown, both illustrating the effect of illumination and colour on the ease with which fine work could be executed.

The first showed the threading of a needle, and the second industrial lathe work. They showed especially that the direction of illumination was even more important than the quality and amount.

The President, in opening the discussion, drew attention to a question ophthalmic surgeons were often asked by patients, namely, what was the best light by which to do a certain type of work. He had personally found that a somewhat difficult question to answer.

Mr. F. A. Williamson-Noble said that he would like to obtain a copy of the artificial lighting chart[1] shown on the screen because he, like the President, was constantly bombarded with the question as to the best light a certain piece of work should be done by. His usual answer was to hand to the inquirer the pamphlet on lighting in schools which gave at the end a table showing the amount of light required for various purposes but that was not so comprehensive as the chart shown during the opening remarks.

With regard to the use of glazed paper in books he personally was constantly bothered by the reflection from the paper and often wondered whether the use of glazed paper should be banned from books. A matt surface would be very much better though that might affect the contrast between the printing ink and the background.

Dr. F. W. Sharpley said he was always finding himself up against the question of glare; although a great deal of work had already been done in that regard much more required to be done. He did not think the effect of glare in everyday life was sufficiently realized. He was not referring particularly to such glare as that caused by specular reflection from glazed paper but, more generally, to the effect of direct light from the source of illumination both in the case of artificial illuminants and natural illumination from the sky through windows. He had noticed in practice so many instances in which glare effect could be reduced by very simple means. It was, to some extent, a matter of educating the public. A matter which might be of interest to ophthalmic surgeons was the question of the more extensive use of eyeshades, such as compositors used, for operations for which they were not now used. One might find, for instance, that a typist was typing against the light, which was obviously wrong, but there were instances in which it was difficult to avoid that position. In such cases an eyeshade would be helpful, to mitigate the effects of glare but one seldom saw it used. It would be interesting to hear what ophthalmic surgeons had to say with regard to the more extensive use of eyeshades.

The use of fluorescent lamps was often recommended as a means of reducing glare because there was a larger source and, consequently, a lower surface brightness for a given candle-power. It did not seem to be as fully appreciated as it might be that that lower brightness did reduce the glare in one sense, but there was still an appreciable degree of glare from the disability point of view, just as there was from a large daylight window. One could easily detect the effect of that glare by simply shading the eyes momentarily from the source while observing an object in the same field of view.

With regard to the flicker from fluorescent lamps, the use of lamps on different phases staggered over the factory system was one way of reducing the flicker though it did not altogether abolish the effect, particularly in the peripheral field of view. The speaker did not think a self-contained three-phase lamp had yet been produced, but such a lamp with a suitable fusing glass would combine the light from each phase and give a single light unit from which there would be no appreciable flicker. Had that been attempted and, if not, were there any real difficulties in the way? He personally could not see any insurmountable difficulties.

---

[1] Procurable from the Illuminating Engineering Society, 32, Victoria Street, London, S.W. Included in "I.E.S. Code for the Lighting of Building Interiors." 1s. 6d.

Much had been said as to the intensity of illumination and instruments for measuring that intensity. It was, of course, widely recognized that intensity was only one aspect of lighting, but it was possibly not fully recognized how small an aspect of the whole it was. It seemed that there should be an endeavour to use the individual himself as a meter for assessing lighting. If it were possible to measure the output of a group of individuals under conditions which were otherwise completely controlled it might be possible to get a better evaluation of lighting effect. The speaker here had in mind output from factories; it was not, of course, possible to measure output, say, from a home. One could, however, conceivably adapt the results obtained from the factory investigation. A measure of output in the factory would take into account the accidents, mistakes and speed of working; it would measure, in a sense, the glare and discomfort effects; it would reflect the psychological effect of the lighting and other factors not taken into account by intensity measurements alone and of which little was known.

Mrs. Dorothy Campbell drew attention to two points: (1) That the clerical staff in a factory are often denied good illumination owing to the expense of installation; and (2) that in the dirtier trades, such as moulding, illumination is allowed to fall deplorably low because the lights are not kept clean.

Mr. D. V. Giri asked for some explanation of what was meant by absorption of light. Also he wanted from the lighting engineers information as to goggles so frequently used now, and of all tints. Did the trade go upon any scientific principle in introducing the tints of the goggles and why should the public resort to them without having any test beforehand? He frequently went to winter sports and had never taken any steps to protect his eyes and, moreover, he had never felt the need for so doing. Many others also went to winter sports and did not need eye protection. In the vast majority of cases that was unnecessary. The tints of the goggles varied so much that the speaker wondered on what basis the manufacturers produced the various tints.

Dr. Brian Stanford said that the point made earlier, that many people found the new fluorescent lighting "a strain" on their eyes, could not be dismissed just because there was no evidence of pathological changes. He thought there was a psychological explanation: If the intensity of ordinary outdoor daylight was assessed as 1,000 to 10,000 units, then in the house it was about 40 units. When it reached 15 to 12 units one switched on the light and as daylight further faded one was working with electric lighting at about 8 units. The colour of the new daylight fluorescent bars matched daylight extremely closely, and in an ordinary room one lamp gives about 12 units, that is an illumination at which one would normally want to switch on the electric light, and yet the lights were on. That sensation might account for the sense of strain complained of; the lights were on and yet one wanted to put them on. If the daylight bar were replaced by the Type B bar, which has a reddish light, then it was accepted as artificial light. The level of illumination was much the same, but one knew that lights were on and felt happier. But one daylight bar in a small kitchen with white walls caused no strain because the level of illumination here reached 20 units.

Mr. Williamson-Noble had referred to glazed paper for books, which raised an interesting point. The reflectivity of good white paper was about 80% and of black ink about 3%, which gave a contrast range of about 30 to 1. In a well-lit room that was too much, but it was necessary for bad lighting conditions. Most homes were ill-lit, but books designed for the richer people who had more brightly lit homes were printed on off-white paper, so bringing the contrast down to about 20 to 1.

The President, after some closing remarks, referred to Mr. Giri's point on the wearing of goggles. He (the President) thought it might be said that goggles were worn often merely as a contrast, just as the black patch was in earlier days!

Section of Proctology

President—A. Hedley Whyte, D.S.O., T.D., M.S., F.R.C.S.

[*March* 12, 1947]

An Explanation of the Difference Between a Papilloma and an Adenoma of the Rectum

By Cuthbert E. Dukes, O.B.E., M.D.

(*Pathologist to St. Mark's Hospital, London*)

Two varieties of benign epithelial tumour occur in the rectum, the villous papilloma and the adenoma. Both arise from the mucous membrane but they seem to develop along different lines so that each comes to have a characteristic appearance and histological structure. A villous papilloma is a soft shaggy tumour, often with rather ill-defined edges, attached by a broad base and extending over a wide area. An adenoma, on the other hand, is a compact rounded mass of glandular tissue, sessile at first but later attached by a relatively narrow pedicle.

The striking difference in gross characters of these two tumours is reflected also in their histology. In a villous papilloma the mucus-secreting epithelium covers the outside of the supporting central core of connective tissue and blood-vessels and the secretion is poured out on the surface, whereas in an adenoma the secreting cells are arranged as in tubular glands and the mucus is therefore discharged into a confined space.

Why should these two tumours, derived from a similar source and composed of identical elements, differ so strikingly both in appearance and intimate structure? The most obvious reply is that the differences are due to the fact that a papilloma projects from the surface and has therefore ample room in which to expand whereas the development of an adenoma is to some extent restricted by the tissues in which it is embedded. This explanation presupposes that a papilloma is derived from surface epithelium whereas an adenoma is derived from epithelium deeper down in the mucous membrane. I think this explanation is the right one and to illustrate it I have prepared two series of diagrams, one representing the proliferation of surface epithelium and the other a similar proliferation of epithelial cells situated at the bottom of the crypts of Lieberkühn.

The first consequence of the proliferation of a group of superficial cells (such as those indicated by shading in fig. 1A) is the formation of a small villous-like projection (fig. 1B). This arrangement is all that is needed to accommodate the twofold increase in cells resulting from their first division, but when the tumour cells divide a second time, resulting in a fourfold increase the central stroma must either become unduly long and fragile or begin to branch as shown in fig. 1C. This is what takes place. Nourishment and support for the eightfold and sixteenfold increase in numbers resulting from the third and fourth division can only be provided by further branching of the stroma as illustrated in fig. 1D and E. Thus the natural consequence of the proliferation of a small group of superficial cells is a tumour with the architecture of a villous papilloma.

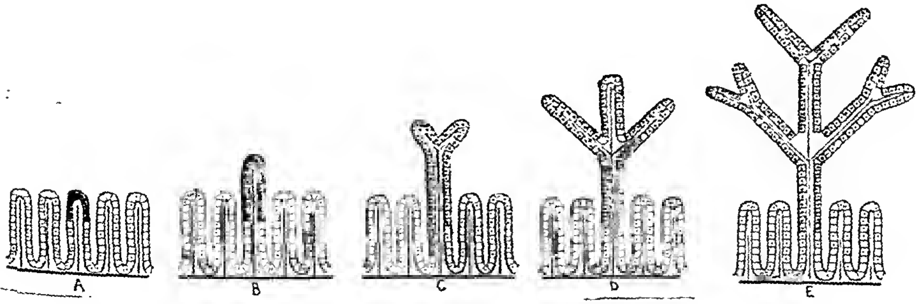


Fig. 1.—Proliferation of superficial glandular epithelium.

Let us now consider what is likely to happen when a similar number of epithelial cells situated in the depths of the mucous membrane begin to divide and to demand room to expand (fig. 2A). The first result will be a compact nodule of new growth embedded in the deeper layers of the submucosa (fig. 2B). The increased space necessitated by this doubling of the cell population can only be gained by encroaching on tissues below and on each side and by bulging from the surface (fig. 2C). A further cell division will result in an acute problem of "Lebensraum". Below and on either side there are obstacles to further expansion and the path of least resistance is obviously upwards to the surface (fig. 2D) Once this is reached there is ample room for the sixteenfold increase resulting from the fourth division (fig. 2E). Finally, any tumour with a narrow base of attachment which projects into the lumen of the bowel tends to become pedunculated because of peristaltic movements and the traction exerted by the passage of intestinal contents over its surface, so I have represented this inevitable rearrangement of the tumour tissue in fig. 2F. This now has the familiar characteristics of a pedunculated adenoma, consisting of a compact rounded mass of glandular tissue attached by a pedicle containing blood-vessels and supporting tissues only.

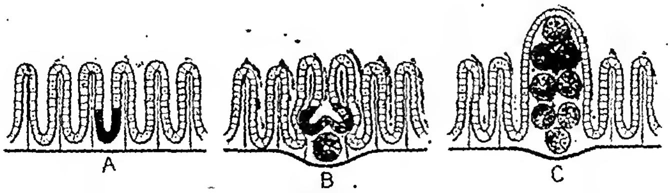


FIG. 2, A, B, C.—Proliferation of deep glandular epithelium.

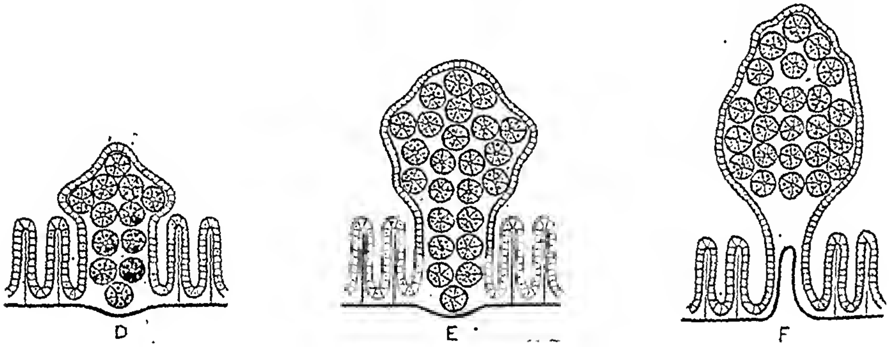


FIG. 2, D, E, F.—Proliferation of deep glandular epithelium.

In constructing these diagrams to illustrate the development of papilloma and adenoma it has been assumed that the cells undergoing proliferation were limited in each case to one small area. Under natural conditions such a narrow restriction of the field of proliferation must rarely occur. None the less it probably is true that the villous papilloma type of growth is the end-result of the action of an agent which has affected *chiefly* the superficial epithelium, whereas an adenoma results when the group of neoplastic cells are situated *chiefly* at a deeper level. In practice we can distinguish tumours which are pure papillomas, others pure adenomas and also an intermediate group which are papillomatous on the surface but adenomatous at the centre.

It may perhaps be thought that the question of the site of origin of these tumours is not of much practical importance and merely another example of the sort of idle speculations in which a pathologist is apt to indulge. But I must remind you that the view is often expressed that an adenoma is more likely to undergo malignant change than a papilloma. Is this really the case? Allowance must first be made for the fact that an adenoma is a much commoner lesion than papilloma and obviously therefore adenomas are much more frequently sectioned. This is certainly the chief reason why it is commoner for carcinoma to be reported in an adenoma. Still, even when allowance has been made for the greater number of adenomatous tumours examined I think it is probably true to say that carcinoma *is* more likely to occur in an adenoma than a papilloma. The most obvious reason for this is that the secretion from a papilloma is poured out on the surface whereas in an adenoma it is discharged into a confined space and therefore liable to be retained, and retention of secretion often acts as a source of irritation. However, although there may be slight differences dependent on considerations such as these it should be said in conclusion that in liability to malignancy there are no fundamental differences between adenomas and papillomas.

Right Hemicolectomy

By E. G. MUIR, M.S., F.R.C.S.

"AT last a case was satisfactorily completed so far as the operation was concerned; but I knew from the first that this was one of the typically malignant class, and that life could not be much prolonged." Thus Paul (1895), the British apostle of large bowel surgery, ended the description of his first successful case of resection and restoration of continuity for a carcinoma of the ascending colon. From that time he put away the decalcified bone tubes with which he had been attempting to anastomose the large bowel and used only the method which bears his name. Though the first successful case in this country was on the right, the Paul or Paul-Mikulicz operation soon became popular on the left colon while other methods were adopted for an ileocæcal resection. Arbuthnot Lane, reputedly a master of technique, who in 1895 dismissed colectomy in his "Manual of Operative Surgery" in a few lines and the note that "Mr. Bryant first performed this operation successfully" ,was in 1909 advising a right, or even larger colectomy for chronic constipation and intestinal toxæmia and relying on intra-abdominal anastomosis without bowel drainage. His usual method was a two-stage resection with a preliminary ileotransverse colostomy. This, or the one-stage resection and anastomosis, has remained the most popular operation in this country. In 1932 Gabriel described the combination of this method with catheter drainage of the colon at the anastomosis. Lahey's revised Paul-Mikulicz operation for right hemicolectomy has recently been advocated by Maingot (1945), who has stressed the safety of this method. The American symposium on colonic surgery published in 1943 gave an interesting cross-section of present American surgical opinion which is by no means in favour of this method, whose necessary defects are the small bowel fistula and the delay in closure. Thus Wangensteen prefers primary resection with end-to-end aseptic anastomosis under constant suction with a duodenal or Millar-Abbot tube for five days. Whipple considers pre- and post-operative decompression with a Millar-Abbott tube and an open anastomosis to be the choice. Jones advises a right end-to-side ileotransverse colostomy with a small catheter inserted into the ileum 6 to 8 in. (15 to 20 cm.) above the anastomosis, but adds that he now prefers a Millar-Abbott tube instead of the catheter. Allen advises the two-stage attack with a preliminary ileotransverse colostomy.

There are certain points in connexion with this operation and indeed all colonic surgery which all surgeons will accept as fact; others depend on individual fancy. Thus, fluid balance and the body requirements, the prevention and treatment of shock, good anæsthesia, bowel chemotherapy before operation, the prevention, early recognition and effective treatment of chest complications are all accepted as important. To Wangensteen, amongst others, surgery owes a debt for the stress laid on intestinal distension, its prevention and treatment; gastric suction is now widely used. The extent of the resection for a right hemicolectomy shows little variation, nor would any now contend that less can be resected by an exteriorization method than by another. On the other hand there are many different methods of anastomosis and suture. Right hemicolectomy cannot always be a planned operation; the conditions requiring it may be discovered unexpectedly or in emergency surgery.

The ideal operation is surely one which permits of a one-stage resection and anastomosis in all but the worst cases; where no secondary operation is required; where no factor making for safety is ignored and provision is made, should an intra-abdominal anastomosis leak, to minimize the disaster.

I believe that the following operation fulfils most of these requirements.

THE OPERATION

I have employed a Millar-Abbott tube in those cases with pre-operative distension and a resection below it gives a pleasant feeling of security but while I have not had the opportunity to use the tube when fitted with a stylet, the ordinary pattern can occasion both irritation and distress to patient and surgeon alike if it takes long to pass through the pylorus. Since other provision is made by this operation it is not used as a routine. Gastric or duodenal tube suction is employed either immediately before, or as soon after operation as possible.

A right paramedian incision is used. After clearing the omentum from the right third of the transverse colon, the part to be resected is mobilized in the usual manner and the mesentery divided. Non-crushing clamps are then applied above and below, that on the ileum being applied, after emptying the bowel as much as possible, some 10 in. (25·4 cm.) above the point of resection. The bowel is removed, ensuring a good blood supply at the point of colonic division. The end of the ileum is now closed and a side-to-side antiperistaltic anastomosis made with the colon 2 in. (5 cm.) distal to the clamp closing the divided end of the colon. This clamp is now oversewn and the divided end of the colon closed except for half a centimetre at that corner farthest from the anastomosis. A soft rubber tube, about the size of a 12 or 13 catheter, but with a rather larger lumen, some 16 in. (40·6 cm.) in length and with lateral holes cut in it for 10 in. (25·4 cm.) from the end, is now inserted through this gap in the end of the colon, through the anastomosis and up the lumen of the ileum. The last lateral hole should lie about 1 in. (2·5 cm.) within the colon. The tube is stitched to the colon and the bowel turned in around it with a number of circular sutures as in a gastrostomy. The soft clamps are now removed and some of the terminal coils of ileum are gently threaded along the rubber ileostomy tube. At the same time suction can be applied to the tube and if there has been any distension some quiet effective decompression of the terminal ileum can be carried out without any harsh treatment of the small bowel. The gap in the mesentery and the raw surface on the posterior abdominal wall are now closed. The omentum is wrapped round the ileostomy tube and the anastomosis.

A small stab incision is now made through the abdominal wall about 2 in. (5 cm.) below the right costal margin and outside the rectus sheath, about the size of that made for a terminal colostomy but without the excision of skin. The peritoneum is opened and its edges held in forceps. The ileostomy tube is now brought out through this incision and the colon around it sutured to the peritoneal edges by a number of interrupted sutures. The skin edges may require a stitch and the tube is anchored to the skin. The abdomen is then closed.

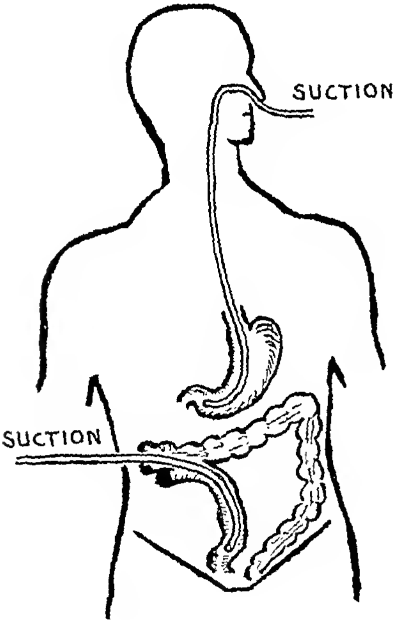


FIG. 1.—Combined gastric and ileal suction drainage.

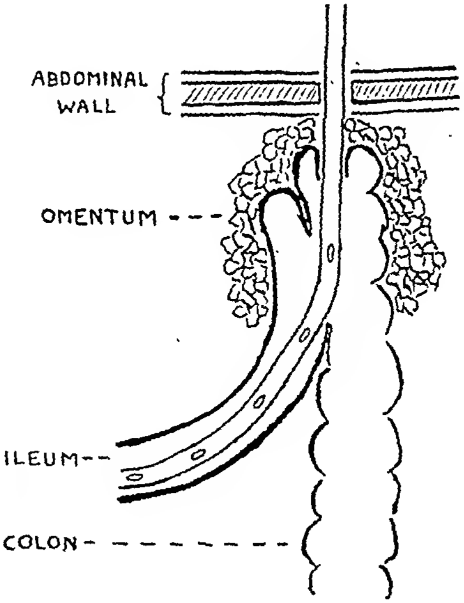


FIG. 2.—Ileostomy tube.

POST-OPERATIVE TREATMENT

In a planned proceeding an intravenous drip is set up before the abdomen is opened. If not, it is commenced either during or immediately after the operation. Apart from the prevention and treatment of shock the patient relies on this route for all his fluid requirements for at least forty-eight hours, that amount being judged sufficient which will approximate a normal urinary output.

Constant suction is applied to both the gastric and ileostomy tubes. The ileostomy tube may become blocked and require gentle syringing through with a little water or saline. Gastric suction is discontinued after forty-eight hours if the ileostomy tube is satisfactory in its drainage and fluids are then started by mouth. The intravenous drip is discontinued when the patient is taking sufficient by mouth.

The ileostomy tube is removed after a week or when it is loose. Some leakage may take place through the wound for a few days, but in a third of my cases no leakage occurred and the longest that an intestinal fistula persisted was a fortnight. No secondary operation has ever been necessary.

I have now performed this operation on twenty cases: Carcinoma 10, Crohn's disease 7, sarcoma 1, volvulus 1, intussusception 1.

There has been no mortality but one post-operative mishap. Here the patient's paramedian incision broke down, a coil of small bowel became lodged in the wound, a small bowel fistula from this coil developed and the wound took three months before it was finally healed.

Comment

I believe this operation has certain advantages and that it is applicable to all but the worst cases. It is a one-stage resection; no second operation to close a fistula is necessary. Though the anastomosis is intraperitoneal it is fixed to the parietal peritoneum beneath an abdominal incision and should sepsis occur within its omental wrappings it has at least an excellent opportunity to reach the exterior. The anastomosis is placed so that it covers the upper part of the "raw" area left by the resection. Not only is decompression drainage provided for the upper part of the alimentary tract by the gastric suction but the lower reaches of the ileum, that danger area in the post-operative case, are also drained and can be emptied considerably at operation. There may be dangers in introducing a rubber tube through an anastomosis, but I have seen no ill-effects. It is perhaps apposite to point out that Wangensteen (1943) has described two cases in which, with a Millar-Abbott tube in the lower ileum, it was yet necessary to put a duodenal tube down the patient's other nostril for post-operative distension. That this can occur once the small bowel has been "swept and garnished" by the passage of a Millar-Abbott tube and with the tube still in position, is surely good evidence of the part played in post-operative distension by aerophagy.

REFERENCES

Allen, A. W. (1943) *Surgery*, 14, 350.
Gabriel, W. B. (1932) *Proc. R. Soc. Med.*, 25, 1016.
Jones, T. E. (1943) *Surgery*, 14, 342.
Lane, W. A. (1895) Operative Surgery, London.
—— (1909) The Operative Treatment of Chronic Constipation, London.
Maingot, R. (1945) *Proc. R. Soc. Med.*, 38, 377.
Paul, F. T. (1895) *Lpool med.-chir. J.*, 15, 374.
—— (1925) Selected Papers, London.
Wangensteen, O. (1943) *Surgery*, 14, 403.
Whipple, A. O. (1943) *Surgery*, 14, 321.

A Small High-grade Carcinoma of the Rectum with Extensive Lymphatic Spread.—W. B. Gabriel, M.S.

R. B., male, aged 48.

History.—His chief complaint was of piles, with latterly more prolapse and some burning pain at defæcation.

Examination on 12.11.45 at St. Mark's Hospital revealed a curious indurated elongated plaque in the left anterior quadrant of the anal canal and extending up the rectal wall for about ½ in. (1·25 cm.). The condition suggested at first a recent thrombosis or possibly an early squamous-cell carcinoma.

Biopsy.—A month later the condition was unchanged and an examination under low spinal anæsthesia was done. An indurated cord of lymphatic spread was felt running up the mesorectum in the left posterior quadrant which strongly indicated the diagnosis of malignancy. A biopsy was done and Dr. C. E. Dukes reported that the tumour was a very undifferentiated type of carcinoma of a high grade of malignancy.

Operation.—On 17.12.45 a laparotomy was done under a nupercaine spinal, 1·2 c.c., with pentothal, gas, oxygen, ether. The liver was smooth but some palpably enlarged glands were felt in the mesorectum on the left side. A perineo-abdominal excision was carried out and uneventful recovery followed, the patient being discharged home on the twenty-sixth post-operative day, 12.1.46.

Pathological findings (Dr. C. E. Dukes).—*Gross characters*: The specimen measured 15 in. (38 cm.). There was no obvious tumour, the only visible abnormality being a small hard ridge in the anal canal and lower third of the rectum over which the mucous membrane was not ulcerated. This ridge could be felt to be in continuity with a thickening around the hæmorrhoidal vessels lying in the perirectal tissues. A cord of hard tissue extended up the course of the hæmorrhoidal vessels for several inches. No papillomata were present but diverticula were seen in the distal end of the pelvic colon.

Microscopic structure: The tumour is a colloid carcinoma, very undifferentiated in character, consisting chiefly of isolated signet cells or clusters of signet cells embedded in mucoid material.

the colon. This clamp is now oversewn and the divided end of the colon closed except for half a centimetre at that corner farthest from the anastomosis. A soft rubber tube, about the size of a 12 or 13 catheter, but with a rather larger lumen, some 16 in. (40·6 cm.) in length and with lateral holes cut in it for 10 in. (25·4 cm.) from the end, is now inserted through this gap in the end of the colon, through the anastomosis and up the lumen of the ileum. The last lateral hole should lie about 1 in. (2·5 cm.) within the colon. The tube is stitched to the colon and the bowel turned in around it with a number of circular sutures as in a gastrostomy. The soft clamps are now removed and some of the terminal coils of ileum are gently threaded along the rubber ileostomy tube. At the same time suction can be applied to the tube and if there has been any distension some quiet effective decompression of the terminal ileum can be carried out without any harsh treatment of the small bowel. The gap in the mesentery and the raw surface on the posterior abdominal wall are now closed. The omentum is wrapped round the ileostomy tube and the anastomosis.

A small stab incision is now made through the abdominal wall about 2 in. (5 cm.) below the right costal margin and outside the rectus sheath, about the size of that made for a terminal colostomy but without the excision of skin. The peritoneum is opened and its edges held in forceps. The ileostomy tube is now brought out through this incision and the colon around it sutured to the peritoneal edges by a number of interrupted sutures. The skin edges may require a stitch and the tube is anchored to the skin. The abdomen is then closed.

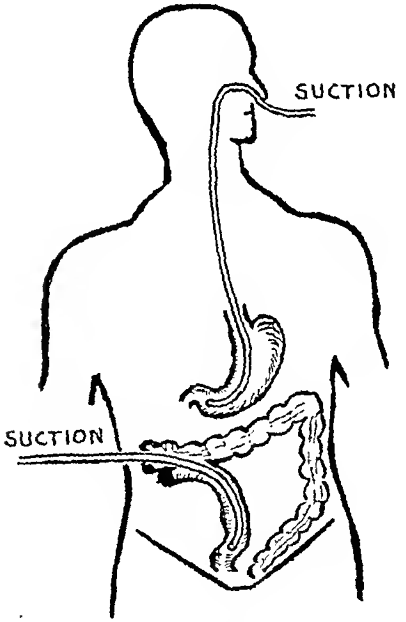


FIG. 1.—Combined gastric and ileal suction drainage.

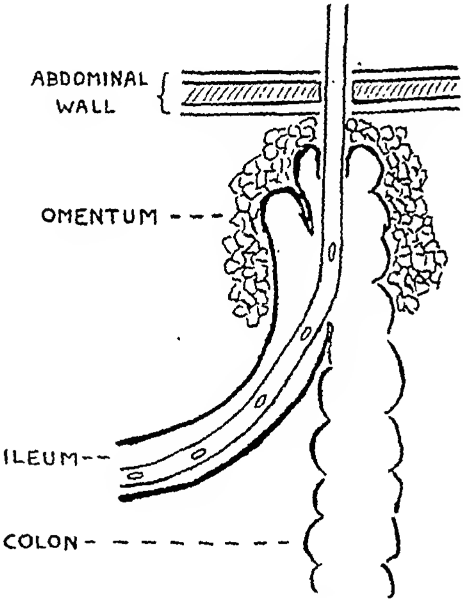


FIG. 2.—Ileostomy tube.

POST-OPERATIVE TREATMENT

In a planned proceeding an intravenous drip is set up before the abdomen is opened. If not, it is commenced either during or immediately after the operation. Apart from the prevention and treatment of shock the patient relies on this route for all his fluid requirements for at least forty-eight hours, that amount being judged sufficient which will approximate a normal urinary output.

Constant suction is applied to both the gastric and ileostomy tubes. The ileostomy tube may become blocked and require gentle syringing through with a little water or saline. Gastric suction is discontinued after forty-eight hours if the ileostomy tube is satisfactory in its drainage and fluids are then started by mouth. The intravenous drip is discontinued when the patient is taking sufficient by mouth.

The ileostomy tube is removed after a week or when it is loose. Some leakage may take place through the wound for a few days, but in a third of my cases no leakage occurred and the longest that an intestinal fistula persisted was a fortnight. No secondary operation has ever been necessary.

Section of Odontology

President—Professor H. STOBIE, F.R.C.S., L.D.S.E.

[*May* 19, 1947]

Unilateral Hypoplasia of Face and Teeth

By Professor EVELYN C. SPRAWSON, M.C., D.Sc., M.R.C.S., L.D.S.

B. B., a male aged 6½ years (fig. 1), presents many abnormalities of a hypoplasic character involving the left side of his face, jaws and teeth, but the condyle itself does not appear to be implicated. All the deciduous molars and most of their successional teeth are absent on the left side. There is no external scarring. He is below average intelligence (I.Q. 79). The abnormality is not familial and there is no history of any difficulty in parturition. The asymmetry was noticed soon after birth.

On examination there is marked asymmetry of the face, so that the left side is flattened and the chin deviates slightly to the left, the deviation being more noticeable during movement. The left mandibular angle is higher than that of the right, but neither is unduly prominent. Both condyles can be felt and are apparently symmetrical and movements normal. The temporal fossæ are symmetrical.

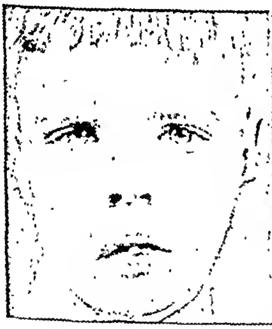


FIG. 1.—Full face.

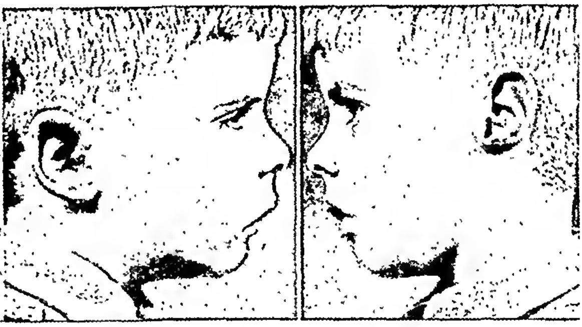


FIG. 2.—Side face.

The left ear (fig. 2) is smaller than the right, is more highly placed, and they are asymmetrical.

In the mouth the left anterior pillar of the fauces passes forward to blend with the loose movable mucous membrane covering the mandibular alveolar ridge; the posterior pillar appears to be normal. The left half of the tongue is markedly smaller than the right, and the tongue deviates to the left on protrusion.

There is no dental caries.

On the right side all the deciduous teeth are present in maxilla and mandible and are normal in size and shape, and the permanent first molars are erupted and in occlusion.

There are only three mandibular deciduous incisors.

In the left maxilla there are only three deciduous teeth, two incisors and a canine.

In the left mandible there are only two deciduous teeth, one incisor and a canine. The left alveolar ridges appear wasted or atrophied in both maxilla and mandible, and shortened antero-posteriorly, the depth of bone in the mandible being very shallow. There is no evidence that there have ever been any deciduous teeth behind the canines in either jaw and the ridges give no indication of any successional permanent teeth and appear as if there is no alveolar bone present. A large hamular process can be felt. Both ridges are placed more medially than is normal.

Methods of spread: (1) *By direct continuity*—The growth had extended by permeation of the lymphatic channels causing a continuous extension along the hæmorrhoidal vessels. (2) *Venous spread*—There was no sign of venous spread. (3) *Lymphatic spread*—Eleven out of fourteen glands removed at dissection contained metastases and so did the gland marked "uppermost" sent separately for examination.

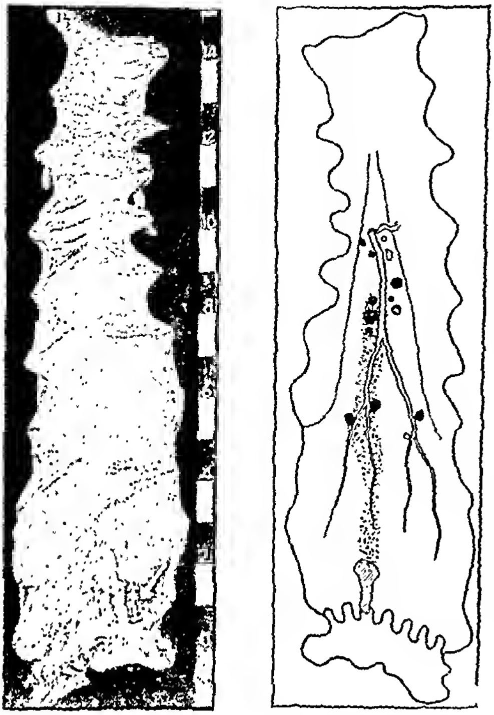


Fig. 1.—A small high-grade carcinoma of the rectum (marked by arrow) with extensive lymphatic spread.

Classification.—Colloid carcinoma of rectum. Extensive lymphatic permeation and twelve glandular metastases. C 2 case.

Subsequent Course.—He remained in fairly good health until 6.5.46, when he reported for examination complaining of some difficulty in micturition. A deep induration in the perineum indicated local recurrence and in addition he presented an enlarged gland in the left groin. He was then referred to St. Bartholomew's Hospital for consideration as to high-voltage X-ray therapy, but when admitted there he was found to have retention with overflow, and cystoscopy showed malignant infiltration of the prostate and bladder. Decompression by an indwelling catheter was required and it was decided that X-ray treatment was contra-indicated.

Re-examination towards the end of June 1946 revealed a very hard irregular fixed mass in the perineum. The patient subsequently went steadily downhill and died of recurrence on 28.8.46, that is, a little over eight months after operation.

Commentary.—The case is of interest from several aspects: (1) The history and clinical findings were anomalous, but the biopsy was of great value in establishing the diagnosis of malignancy; the histological grading rightly indicated a bad prognosis.

(2) The presence of palpable extrarectal spread was revealed by digital examination of the rectum prior to operation and the grave prognosis which accompanies this finding was confirmed by the progress of the case.

(3) Although the primary growth was extremely small, early and extensive lymphatic spread had taken place by the time operation was undertaken and the rapid onset of recurrence shows that even then the growth was surgically inoperable.

Carcinoma of the Paroophoron, invading the Rectum.—A. LAWRENCE ABEL, M.S.

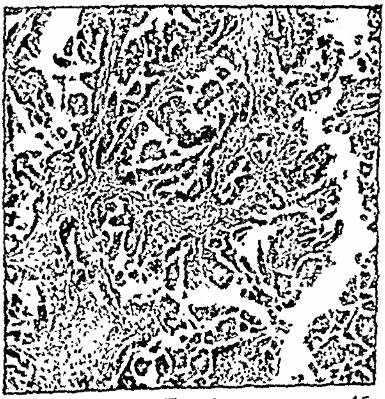


Fig. 1 × 45.

Female, aged 66.

History.—Difficulty in defæcation and occasional slight rectal incontinence for three months, with recent vaginal discharge of blood-stained fluid.

Examination.—P.V.: Ulcer crater in the posterior fornix which was closely adherent to the rectum. Biopsy showed a papilliform adenocarcinoma.

Operation.—Wertheim's panhysterectomy and abdomino-perineal resection of the rectum.

Specimen.—The lower sigmoid rectum and anal canal with the attached uterus and its adnexa and vagina (shown at the meeting).

Histology (Dr. L. Woodhouse Price). — Shows the general structure of a malignant ovarian cystadenoma (fig. 1).

Diagnosis.—Carcinoma of the paroophoron, invading the rectum.

(The report of this meeting will be concluded in the December issue of the Proceedings.)

Section of Odontology

President—Professor H. Stobie, F.R.C.S., L.D.S.E.

[*May* 19, 1947]

Unilateral Hypoplasia of Face and Teeth

By Professor Evelyn C. Sprawson, M.C., D.Sc., M.R.C.S., L.D.S.

B. B., a male aged 6½ years (fig. 1), presents many abnormalities of a hypoplasic character involving the left side of his face, jaws and teeth, but the condyle itself does not appear to be implicated. All the deciduous molars and most of their successional teeth are absent on the left side. There is no external scarring. He is below average intelligence (I.Q. 79). The abnormality is not familial and there is no history of any difficulty in parturition. The asymmetry was noticed soon after birth.

On examination there is marked asymmetry of the face, so that the left side is flattened and the chin deviates slightly to the left, the deviation being more noticeable during movement. The left mandibular angle is higher than that of the right, but neither is unduly prominent. Both condyles can be felt and are apparently symmetrical and movements normal. The temporal fossæ are symmetrical.

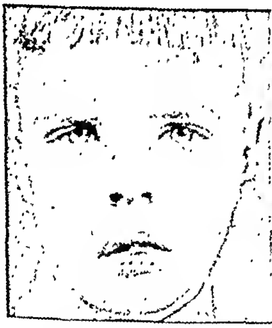


Fig. 1.—Full face.

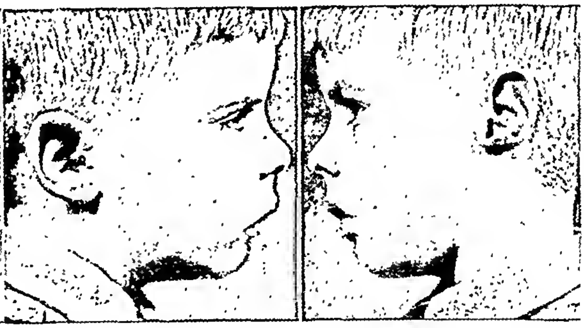


Fig. 2.—Side face.

The left ear (fig. 2) is smaller than the right, is more highly placed, and they are asymmetrical.

In the mouth the left anterior pillar of the fauces passes forward to blend with the loose movable mucous membrane covering the mandibular alveolar ridge; the posterior pillar appears to be normal. The left half of the tongue is markedly smaller than the right, and the tongue deviates to the left on protrusion.

There is no dental caries.

On the right side all the deciduous teeth are present in maxilla and mandible and are normal in size and shape, and the permanent first molars are erupted and in occlusion.

There are only three mandibular deciduous incisors.

In the left maxilla there are only three deciduous teeth, two incisors and a canine.

In the left mandible there are only two deciduous teeth, one incisor and a canine. The left alveolar ridges appear wasted or atrophied in both maxilla and mandible, and shortened antero-posteriorly, the depth of bone in the mandible being very shallow. There is no evidence that there have ever been any deciduous teeth behind the canines in either jaw and the ridges give no indication of any successional permanent teeth and appear as if there is no alveolar bone present. A large hamular process can be felt. Both ridges are placed more medially than is normal.

Methods of spread: (1) *By direct continuity*—The growth had extended by permeation of the lymphatic channels causing a continuous extension along the hæmorrhoidal vessels. (2) *Venous spread*—There was no sign of venous spread. (3) *Lymphatic spread*—Eleven out of fourteen glands removed at dissection contained metastases and so did the gland marked "uppermost" sent separately for examination.

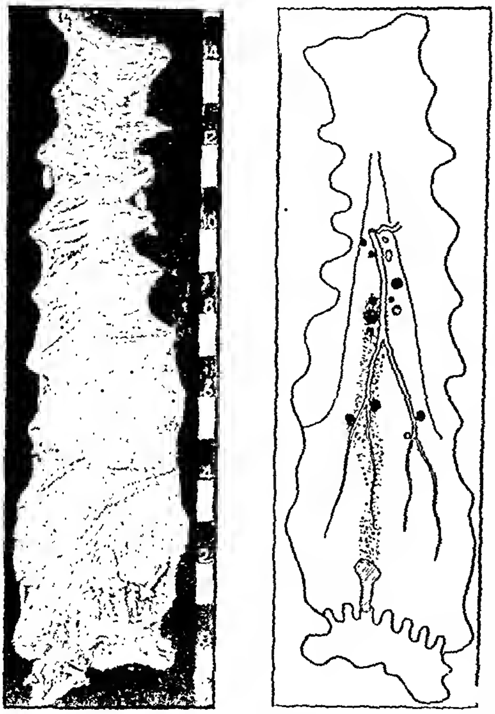


FIG. 1.—A small high-grade carcinoma of the rectum (marked by arrow) with extensive lymphatic spread.

Classification.—Colloid carcinoma of rectum. Extensive lymphatic permeation and twelve glandular metastases. C 2 case.

Subsequent Course.—He remained in fairly good health until 6.5.46, when he reported for examination complaining of some difficulty in micturition. A deep induration in the perineum indicated local recurrence and in addition he presented an enlarged gland in the left groin. He was then referred to St. Bartholomew's Hospital for consideration as to high-voltage X-ray therapy, but when admitted there he was found to have retention with overflow, and cystoscopy showed malignant infiltration of the prostate and bladder. Decompression by an indwelling catheter was required and it was decided that X-ray treatment was contra-indicated.

Re-examination towards the end of June 1946 revealed a very hard irregular fixed mass in the perineum. The patient subsequently went steadily downhill and died of recurrence on 28.8.46, that is, a little over eight months after operation.

Commentary.—The case is of interest from several aspects: (1) The history and clinical findings were anomalous, but the biopsy was of great value in establishing the diagnosis of malignancy; the histological grading rightly indicated a bad prognosis.

(2) The presence of palpable extrarectal spread was revealed by digital examination of the rectum prior to operation and the grave prognosis which accompanies this finding was confirmed by the progress of the case.

(3) Although the primary growth was extremely small, early and extensive lymphatic spread had taken place by the time operation was undertaken and the rapid onset of recurrence shows that even then the growth was surgically inoperable.

Carcinoma of the Paroophoron, invading the Rectum.—A. LAWRENCE ABEL, M.S.

Female, aged 66.

History.—Difficulty in defæcation and occasional slight rectal incontinence for three months, with recent vaginal discharge of blood-stained fluid.

Examination.—*P.V.*: Ulcer crater in the posterior fornix which was closely adherent to the rectum. Biopsy showed a papilliform adenocarcinoma.

Operation.—Wertheim's panhysterectomy and abdomino-perineal resection of the rectum.

Specimen.—The lower sigmoid rectum and anal canal with the attached uterus and its adnexa and vagina (shown at the meeting).

Histology (Dr. L. Woodhouse Price). — Shows the general structure of a malignant ovarian cystadenoma (fig. 1).

Diagnosis.—Carcinoma of the paroophoron, invading the rectum.

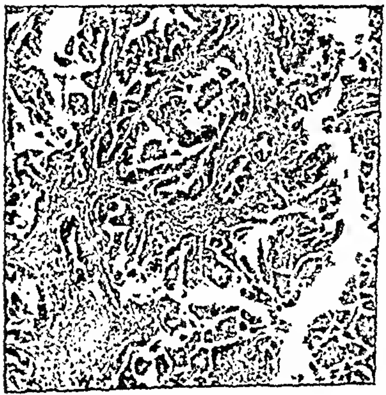


FIG. 1 × 45.

(The report of this meeting will be concluded in the December issue of the Proceedings.)

A Note on Ten Romano-British Skulls from a Burial Ground at Compton, Berkshire

By Sir FRANK COLYER, K.B.E., LL.D., F.R.C.S.

DURING the years 1945-46 a Romano-British burial ground at Roden Down, Compton, Berkshire, was excavated by Mr. M. S. F. Hood and Mrs. Walton and the remains of the skeletons—ten in number—were presented by the owner of the land Mr. J. Trevor, to the Royal College of Surgeons.

The burial ground is 75 feet long and 50 feet wide and is made up of two enclosures. Mr. Hood informs me that during the excavations two cremation hearths were discovered and that these "were in use at some point during the first and early second centuries A.D. After they went out of use the area where they had been was surrounded by the first enclosure which consisted of a ditch with slight banks on either side". The date of the enclosure was approximately the middle of the second century. About the beginning of the fourth century the enclosure was used for burials and three skeletons were found in the area. At a later date a second enclosure was added which was also surrounded by a ditch and shallow banks, in this seven burials were unearthed, the internments dating from about the middle to the end of the fourth century. Mr. Hood suggests that in view of the small number of graves it seems possible that the whole cemetery belonged to one family.

The remains of the burials were examined by Professor F. Wood Jones in relation to sex and age, the measurements of the skulls and the femora by Dr. Lunn.

The dental conditions of the skulls are given below.

Grave 1.—Female, aged 40 to 45. The date of the burial was the early part of the fourth century. In the maxillæ, fig. 1, the right incisor is absent and the canine is in contact with the first incisor. The second premolars, first molars and the left second molar have been lost from parodontal disease and there has been considerable loss of the bone between the left second and third molars and on the posterior aspect of the right third molar. In the mandible the left first premolar is represented by a root, the second premolar has tilted forwards and the crown is close to the canine. Extensive destruction of the alveolar bone is noticeable around the molars, the loss being especially marked on the inner aspects of the left teeth. Calculus is present on the external surfaces of the teeth, the largest deposit being on the incisors.

In occlusion the teeth meet "edge-to-edge" and show a fair degree of attrition.

The posterior surface of the right maxillary second molar has been attacked by caries and there is a cavity in the root of the tooth. As already stated the greater part of the interdental bone between the second and third molars has been destroyed and it is evident that the caries started in the cement about the region of the cervix.

An idea of the septic condition of the mouth of this individual can be formed from the view of the left teeth shown in fig. 2.

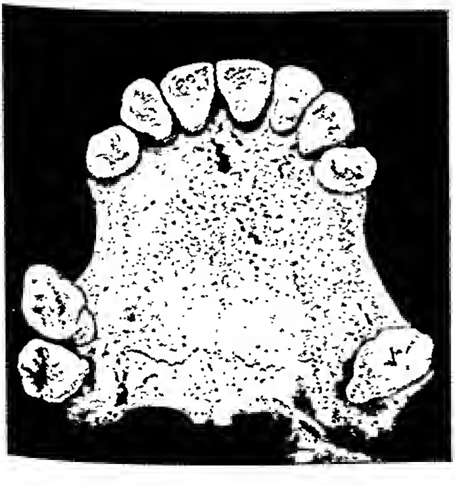


FIG. 1.

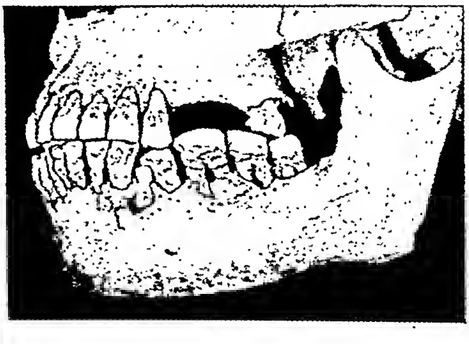


FIG. 2.

FIG. 1.—The maxillary teeth of a female, aged 40 to 45. The right second incisor is absent.

FIG. 2.—View of the left teeth of a female, aged 40 to 45.

Grave 2.—Female, aged 40 to 45. Date of burial, the early part of the fourth century. In this skull all the teeth are present with the exception of the maxillary third molars which

Radiologically (fig. 3) the left coronoid process is absent and there appears to be failure of neighbouring bone growth, which may also account for the left eye appearing to open wider than the right (*see* fig. 1).

On the right side (fig. 4) both bony and dental development appear to be normal for a boy of his age.

On the left side (fig. 5) the only teeth to be seen are:

Deciduous $\left.\frac{|\text{ABC}}{|\ \text{BC}}\right\}$erupted. Permanent $\left.\frac{|1\ 345}{|\ 23}\right\}$unerupted.

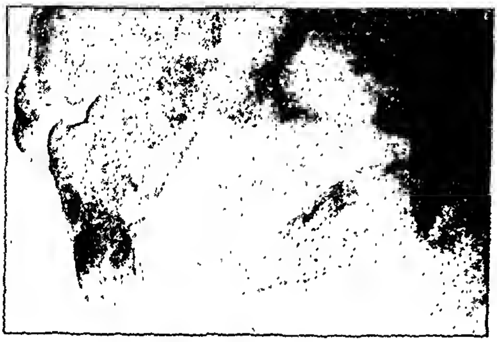


FIG. 3

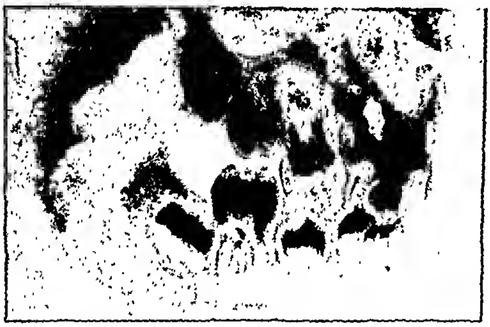


FIG. 4

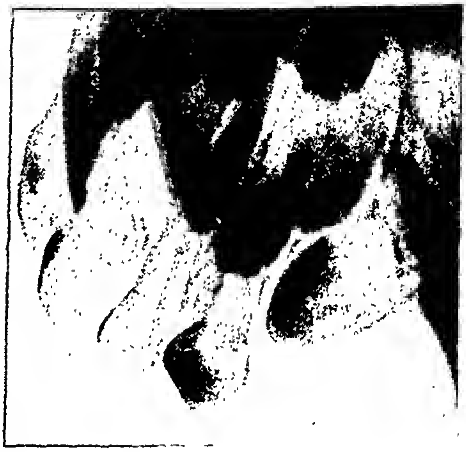


FIG. 5

X-rays: Fig. 3 left mandible; fig. 4 right mandible; fig. 5 left maxilla.

The maxillary second premolar appears to be misplaced and directed towards the deciduous canine. From visual and radiological evidence the size and shape of all teeth on the left side appear to be normal. Just in front of the angle of the mandible it appears as if a molar might be going to develop, but it is very doubtful. There are only three mandibular permanent incisors. The antra are almost symmetrical, that on the left being perhaps slightly larger. The abnormalities appear to be developmental errors having origin partly from the first and partly from the second branchial arch, though, as Rushton has pointed out, not all structures so derived are involved.

Three cases of unilateral hyperplasia of the face, accompanied by enlargement of teeth on the affected side have been recorded by Rushton (1937, 1942) and Miles (1944) during the past ten years, and others recorded earlier make up the total to some eight cases.

In another paper Rushton (1944), referring to unilateral hypoplasia of the mandibular condylar process of congenital origin, states that there may be incomplete or delayed eruption of the molar teeth on the affected side, and that it is generally accompanied by a number of other defects involving the ear and neighbouring parts.

REFERENCES

MILES, A. E. W. (1944) *Brit. dent. J.*, 77, 197.
RUSHTON, M. A. (1937) *Brit. dent. J.*, 62, 572.
—— (1942) *Amer. J. Ortho. and Oral Surg.*, 28, 54.
—— (1944) *Brit. dent. J.*, 76, 57.

A Note on Ten Romano-British Skulls from a Burial Ground at Compton, Berkshire

By Sir FRANK COLYER, K.B.E., LL.D., F.R.C.S.

DURING the years 1945-46 a Romano-British burial ground at Roden Down, Compton, Berkshire, was excavated by Mr. M. S. F. Hood and Mrs. Walton and the remains of the skeletons—ten in number—were presented by the owner of the land Mr. J. Trevor, to the Royal College of Surgeons.

The burial ground is 75 feet long and 50 feet wide and is made up of two enclosures. Mr. Hood informs me that during the excavations two cremation hearths were discovered and that these "were in use at some point during the first and early second centuries A.D. After they went out of use the area where they had been was surrounded by the first enclosure which consisted of a ditch with slight banks on either side". The date of the enclosure was approximately the middle of the second century. About the beginning of the fourth century the enclosure was used for burials and three skeletons were found in the area. At a later date a second enclosure was added which was also surrounded by a ditch and shallow banks, in this seven burials were unearthed, the internments dating from about the middle to the end of the fourth century. Mr. Hood suggests that in view of the small number of graves it seems possible that the whole cemetery belonged to one family.

The remains of the burials were examined by Professor F. Wood Jones in relation to sex and age, the measurements of the skulls and the femora by Dr. Lunn.

The dental conditions of the skulls are given below.

Grave 1.—Female, aged 40 to 45. The date of the burial was the early part of the fourth century. In the maxillæ, fig. 1, the right incisor is absent and the canine is in contact with the first incisor. The second premolars, first molars and the left second molar have been lost from parodontal disease and there has been considerable loss of the bone between the left second and third molars and on the posterior aspect of the right third molar. In the mandible the left first premolar is represented by a root, the second premolar has tilted forwards and the crown is close to the canine. Extensive destruction of the alveolar bone is noticeable around the molars, the loss being especially marked on the inner aspects of the left teeth. Calculus is present on the external surfaces of the teeth, the largest deposit being on the incisors.

In occlusion the teeth meet "edge-to-edge" and show a fair degree of attrition.

The posterior surface of the right maxillary second molar has been attacked by caries and there is a cavity in the root of the tooth. As already stated the greater part of the interdental bone between the second and third molars has been destroyed and it is evident that the caries started in the cement about the region of the cervix.

An idea of the septic condition of the mouth of this individual can be formed from the view of the left teeth shown in fig. 2.

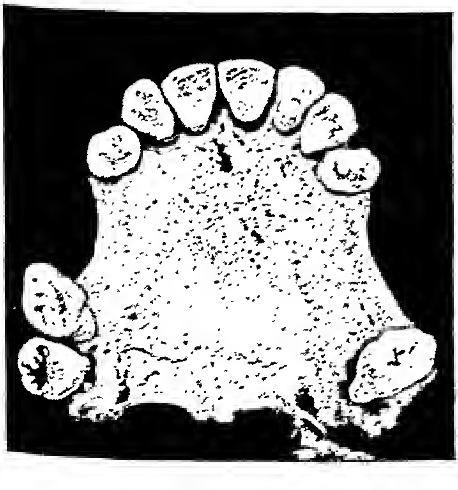


FIG. 1.

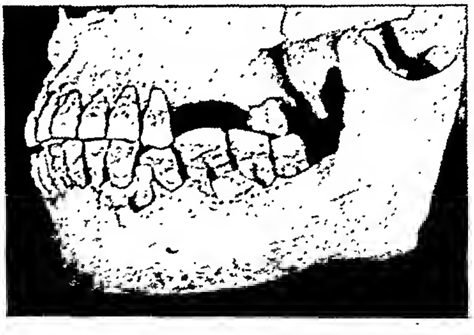


FIG. 2.

FIG. 1.—The maxillary teeth of a female, aged 40 to 45. The right second incisor is absent.

FIG. 2.—View of the left teeth of a female, aged 40 to 45.

Grave 2.—Female, aged 40 to 45. Date of burial, the early part of the fourth century. In this [illegible] teeth are present with the exception of the maxillary third molars which are absent. There is a slight degree of "crowding" of the mandibular incisors and canines, the latter teeth are rotated. In occlusion the maxillary incisors overlap the mandibular teeth.

The alveolar process exhibits a slight but regular recession and there is no rarefaction beyond the margin of the bone. A small deposit of calculus is present on the external surfaces of the teeth all of which show a fair degree of attrition.

Grave 3.—Male, aged 40 to 45. The date of the burial about the middle part of the fourth century. This skull exhibits several interesting variations:

(1) The left maxillary third molar is absent.

(2) The mandibular left third molar is not present but from the appearance of the bone it is not possible to determine whether the tooth was lost from disease or had not developed.

(3) The maxillary second molars are slightly abnormal in shape, they are compressed in the antero-posterior direction.

(4) In the mandible the left second incisor and the canine are transposed. The second incisor, as will be seen from fig. 3, is rotated to a degree sufficient to bring the internal surface of the tooth against the anterior surface of the first premolar.

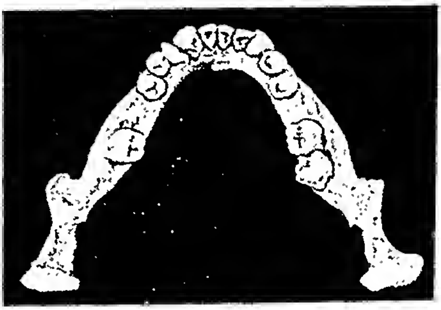


FIG. 3.—Mandible of a male, aged 40 to 45. The left second incisor and canine are transposed.

(5) The maxillary incisors are a little abnormal in position; the mandibular right canine is rotated, the internal surface is in contact with the distal surface of the second incisor.

(6) The mandibular right third molar is tilted against the posterior surface of the second molar and there is a deep "pocket" between the teeth.

In occlusion the incisors meet practically "edge-to-edge", the teeth, with the exception of the maxillary first incisors, show but little attrition. A small deposit of calculus is present on the teeth; the alveolar bone may be regarded as normal.

Grave 4.—Female, aged 65 to 70. Date of burial, the late fourth century. The mandible is edentulous. The maxillæ (fig. 4) are unfortunately defective but the condition of the bone shows that at the time of death the following teeth were present:

$$\underline{3\ \text{x} \mid 12345}\ .$$

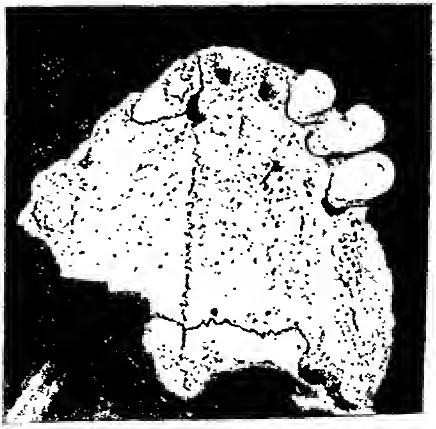


FIG. 4.—Portion of the maxillæ of a female, aged 65 to 70. The right canine is misplaced.

The right canine is misplaced in a horizontal direction, the root, when the premolars were in position, was on the inner aspect of these teeth.

Grave 5.—Female, aged 50 years to a little more. The date of the burial was about the middle of the fourth century. The maxillæ are so defective that it is not possible to form an idea of the state of the dentition. Five maxillary teeth, much worn, were recovered from the coffin, a second incisor, two canines, a premolar and a molar.

The portion of the mandible posterior to the right first premolar is missing. The left second premolar, first and second molars have been lost. In the region of the first incisors there were three teeth, the one next to the right second incisor is in position, the root alone remains of the one next to the left second incisor and between these teeth there is a gap which was occupied by the third tooth. The teeth have been subjected to considerable wear and the alveolar bone shows an advanced stage of destruction.

Grave 6.—Female, aged 55 to 60. The date of the burial is uncertain. The dentition is complete with the exception of the left maxillary first molar which has been lost and of the left second premolar, the root of which alone remains.

There is a slight degree of "crowding" of the mandibular incisors. The teeth show a fair degree of attrition, the condition of the alveolar bone, taking into consideration the age of the woman, may be regarded as normal.

Grave 7.—Male, aged 50 years to a little more. The date of burial was about the last quarter of the fourth century. The following teeth have been lost: The right maxillary first and second molars, the left maxillary third molar and the mandibular molars. The left maxillary first and second molars are represented by roots and the mandibular left first molar is split in a vertical direction leaving the roots separate. The portion of the crown covering the anterior root has been lost and there is an abscess cavity in the bone over the apex of the root. The anterior aspect of the right maxillary third molar has been attacked by caries and a small cavity is present in the root near the cervix.

The teeth exhibit a considerable amount of wear, the occlusal surfaces of the premolars being entirely bared of enamel. The disintegration of the left maxillary molars and the mandibular left first molar is due to the extreme attrition and it is to that cause the loss of the teeth is to be attributed. In occlusion the bite is "edge-to-edge".

Considerable portions of the roots of the cheek teeth are exposed but there is no rarefaction of the bone in the maxillæ and none in the mandible. Calculus is present in fair quantity on the premolars and molars and there is a small deposit on the incisors.

Grave 8.—Male, aged 35 to 40. The burial was probably towards the end of the fourth century. The dentition is almost perfect with the exceptions that there is a slight "crowding" of the mandibular incisors and that the maxillary third molars occlude just internal to their normal relationship with the mandibular teeth. The teeth show but a slight degree of wear and the maxillary incisors overlap the mandibular teeth. The alveolar bone is normal. A view of the teeth is shown in figs. 5A and 5B.

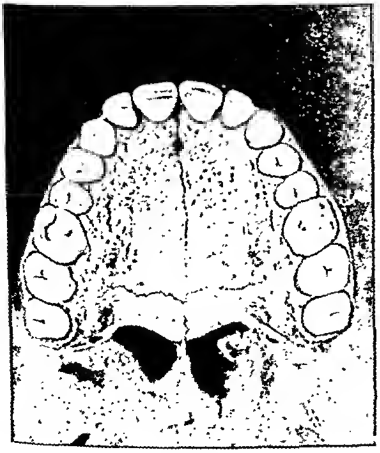


FIG. 5A.

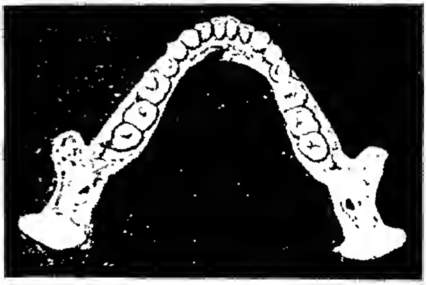


FIG. 5B.

FIG. 5 A and B.—The maxillary and mandibular teeth of a male, aged 35 to 40; date about the end of the fourth century.

Grave 9.—Female, aged 18 to 20. The date of burial was probably the late fourth century. The mandibular third molars are absent and the maxillary third molars are unerupted. The arch of the maxillary teeth is somewhat narrow but there is ample room for the premolars. The left maxillary first premolar is rotated slightly but the abnormality is not due to insufficient room in the arch. In occlusion the maxillary incisors overlap those of the mandible; the alveolar bone is normal.

Grave 10.—Male, aged 50 to 60. The date of burial was well towards the end of the fourth century. The coins with the remains were the latest datable found with the burials. In this skull the right maxillary third molar has been lost and the root alone remains of the left maxillary second premolar. The teeth, with the exception of the incisors, show but little wear and the alveolar bone is in good condition. Calculus is present on the external surfaces of the teeth, the largest deposit being on the incisors. The mandibular left canine and the premolars are slightly abnormal in position, the incisors in occlusion are "edge-to-edge".

Such then are the brief details of the dental condition of these ten skulls from the Compton burial ground. The chief feature is the comparatively large number of variations in the series. In four of the skulls teeth are absent, in one there is an extra incisor in the mandible, in one there is a marked displacement of a maxillary canine, in one the mandibular left second incisor and canine are transposed and the right third molar tilted, facts which suggest instability of the tooth band.

Another feature is the varying degree of attrition of the teeth, for example in skulls 8 and 3 the teeth are very little worn while in skulls 1 and 7 the wear is marked. The amount of parodontal disease varies, in skull 1, a female aged 40 to 45, and in skull 7, a male about 50 years of age, there is evidence of marked destruction of the alveolar bone, on the other hand in skull 6, a female aged 55 to 60, the bone may be regarded as normal for a person of that age.

I may be wrong in my surmise but there would appear to have been a marked difference in the hygienic condition of the mouths of the various individuals. In skulls 2 and 7 the condition of the dental tissues suggests a fairly clean mouth but in skulls 1 and 5 the mouths must have been in a thoroughly septic state. It is tempting to speculate whether this difference in the hygiene of the mouth is related to a difference in the social status of the individuals.

Section of Epidemiology and State Medicine

President—H. J. Parish, M.D., F.R.C.P.E., D.P.H.

[*March* 28, 1947]

Malaria Control with D.D.T. on a National Scale—Greece, 1946.

[*Abridged*]

By J. M. Vine, M.B., B.S.Melb., D.P.H.Eng.

(*Chief, Greece Mission, World Health Organization Interim Commission; late Director, Health Division, UNRRA Greece Mission,* 1946)

Résumé.—Quand cette lutte fut entreprise la situation en Grèce avait déjà été étudiée en détail, et il existait donc une collection abondante de données biologiques, géologiques, météréologiques et entomologiques. Avec la collaboration de l'Ecole d'Hygiène grecque, UNRRA fit des travaux préliminaires avec le DDT en 1945, suivis par une attaque à fond sur les moustiques hibernants pendant l'hiver et sur les insectes adultes pendant le printemps et l'été de 1946, employant uniquement le DDT.

Quatre préparations furent employées: (*a*) une solution à 5% dans le kérosène à l'intérieur des bâtiments, (*b*) une émulsion aqueuse à 26% diluée au cinquième, pour l'intérieur des bâtiments, les meubles et la literie, (*c*) une solution à 5% dans le mazout pour les bâtiments extérieurs et autres refuges de moustiques, (*d*) une solution à 20% dans le velsicol NR 70, en forme d'aérosol distribué par avion, ou diluée avec du mazout pour donner une concentration de 5% de DDT pour vaporisation à la main des dépendances.

La population a coopéré volontiers, non seulement à cause de la réduction des moustiques mais aussi en raison de l'effet secondaire sur d'autres insectes nuisibles. Ce détail est très important dans les campagnes de ce genre.

Le résultat de cette attaque fut une diminution marquée de l'incidence du paludisme pendant cette saison, d'après le taux parasitaire, l'incidence infantile et l'index splénique. Des villages non traités servant de contrôles ont prouvé que l'an 1946 ne fut pas une saison de basse incidence naturelle en Grèce. Le gouvernement a voté sans hésiter la même affectation de fonds pour l'an 1947.

Leçons essentielles: (1) Il est nécessaire de connaître la situation en détail avant d'établir les plans d'attaque. Le problème du paludisme varie d'un pays à un autre, et dans les différentes régions d'un pays.

(2) L'importance des plans détaillés et de la coopération sans réserve du gouvernement central et local, des malariologistes, des ingénieurs et inspecteurs de l'administration sanitaire, des officiers d'approvisionnement et de transport, des fonctionnaires de finance et, surtout, de la population.

(3) L'opération doit être exécutée d'une façon régulière, et le moment doit être choisi selon les habitudes des anophèles.

(4) L'information publique par la propagande, les imprimés, les journaux et la radio est essentielle.

(5) Il est avantageux de lancer une dernière attaque sur les lieux de reproduction à la fin de la saison, pour diminuer le nombre de moustiques hibernants ayant accumulé de la graisse.

(6) Il faut des recherches supplémentaires sur divers aspects du DDT, sur les substances les plus appropriées pour la préparation d'émulsions, la détermination du contenu *para-para* de diverses produits commerciaux, l'effet d'une chaleur continue sur la préservation, et sur le matériel le plus approprié pour les récipients.

(7) Ces questions restent à répondre: "Quel est l'effet du des quantités et des concentrations de DDT employées dans ces expériences sur les anophèles adultes?" et "Quel est le temps de contact nécessaire pour assurer une efficacité de 100% avec diverses concentrations de vaporisation résiduelle par unité de superficie?"

(8) Il reste beaucoup de recherches expérimentales, techniques et entomologiques à faire pour trouver la méthode la plus efficace et la plus économe d'employer le DDT dans la lutte anti-malarienne.

(9) Les valeurs relatives de la vaporisation des maisons pour exterminer les insectes adultes et des mesures larvicides ou des deux ensemble ne peut être décidée que par la considération des conditions locales et par des expériences locales pendant plusieurs saisons.

(10) L'effet toxique du DDT sur l'homme est négligible, mais, d'après l'observation de 6000 travailleurs employés pendant les six mois de l'été, il est nécessaire de protéger la peau contre les infections dues au kérosène et à l'huile employés comme diluents.

Extracto.—Grecia, donde existian gran cantidad de datos biológicos, geológicos, metereológicos y entomológicos, fué de los paises en que se llevó tempranamente a cabo la lucha antipalúdica en gran escala. Ya en 1945, la UNRRA, conjuntamente con la Escuela Griega de Higiene, realizó un trabajo preliminar con DDT contra los mosquitos invernadores durante los meses de invierno, que, después, en la primavera y verano de 1946, se extendió a mosquitos adultos y larvas. Para ello se usó DDT como única arma.

Fueron empleados cuatro distintos preparados de DDT: (*a*) Al 5% en petróleo para el interior de las viviendas; (*b*) Al 26% en emulsión acuosa, diluida cinco veces, usada en interiores, mobiliario, colchones y ropas de cama; (*c*) Al 5% en aceite Diesel para los exteriores de las casas y lugares ocupados por los mosquitos; (*d*) Al 20% en velsicol NR 70, empleado como aerosol para ser lanzado desde aeroplanos, o también diluido en aceite Diesel al 5% DDT, para rociar el exterior de las viviendas.

La población cooperó, no solamente por lo que la lucha contra el mosquito representaba, sinó también porqué el efecto beneficioso alcanzaba a librarles de otros molestos insectos domésticos. Este es el punto mas valioso de tales campañas.

Los resultados, determinados por la proporción de parásitos, proporción de niños afectos e índice esplénico, mostraron un decidido descenso en el número de casos de paludismo, mientras que, por las cifras obtenidas en aldeas usadas como controles, y por tanto, no tratadas, quedó demostrado que el 1946 no fué un año de naturalmente baja incidencia en Grecia. El Gobierno griego, sin vacilación alguna, adoptó para 1947 las mismas medidas adoptadas en 1946.

Enseñanzas obtenidas: (1) Importancia de recoger datos lo más completos posible antes del planeamiento de las operaciones. El problema del paludismo difiere no solo entre las diversas regiones, sino también entre las distintas partes de una misma región.

(2) Importancia del planeamiento detallado en completa colaboración cón las autoridades gubernamentales, tanto centrales como locales, servicios antipalúdicos, de saneamiento e inspección, provisión de materiales y transporte, servicios financieros y, especialmente, cooperación de la población local.

(3) Las operaciones deben ser realizadas uniformemente y con oportunidad, considerando los hábitos del anopheles.

(4) Es de esencial importancia la informacion pública por medio de folletos de propaganda, prensa y radio.

(5) Ventajas de realizar un ataque intenso contra los criaderos de mosquitos al final de la estación, con el objeto de disminuir el número de insectos que invernan a expensas de sus reservas de grasa.

(6) Se requiere ademas ulterior investigación sobre varios aspectos del DDT: cuales son los agentes más efectivos para la preparación de emulsiones; determinación del contenido en *para-para* de los distintos productos comerciales; efecto del calor prolongado durante el almacenamiento y tipos de envase mas apropiados.

(7) Quedan todavia por dilucidar las siguientes preguntas: ¿Que efecto tienen sobre el anopheles las diferentes concentraciones y cantidades empleadas por área de superficie? y ¿Cual es el tiempo de contacto mínimo para obtener una efectividad de un 100% con diferentes concentraciones de DDT por área de superficie?

(8) Deben realizarse grandes trabajos experimentales, técnicos y entomológicos antes de poder determinar las mejores condiciones de uso del DDT, en cuanto a eficacia y economía se refiere.

(9) El valor de las pulverizaciones en el interior de las casas, comparado con la exterminación de las larvas o, con una combinacion de ambos procedimientos, puede unicamente ser decidido considerando las condiciones locales y solo después de haber estado experimentando durante varias temporadas en la misma localidad.

(10) El efecto tóxico del DDT sobre los seres humanos es tan insignificante que puede ser despreciado. Deben, sin embargo, tomarse precauciones para proteger la piel contra las infecciones debidas al petróleo o al aceite usados como vehículo. Esta conclusión viene demostrada por la observación de 6000 obreros empleados durante los seis meses de verano.

КОНСПЕКТ.—В предыдущие годы в Греции была поизведена тщательная исследовательная работа. Были собраны обширные данные — биологические, геологические, метеорологические и энтомологические. УНРРА, совместно с греческой школой гигиены, произвела предварительную работу с Д.Д.Т. в 1945-ом году. В течении зимы удалось, пользуясь одним только Д.Д.Т., справиться с зимующими насекомыми, а весной и летом 1946-го года тем же путем были уничтожены как насекомые, так и их личинки.

При этом употреблялось четыре различных препарата Д.Д.Т.: а/ 5% раствор в керосине для внутренних помещений; б/ 26% водянистая эмульсия, растворенная в 5 раз, для внутренних помещений, для мебели и постельного белья; в/ 5% раствор в Дизельном масле для наружных помещений и для других мест, куда садится комары; г/ 20% раствор в версиколе HP70 в виде аэрозола посредством аэропланов, а также разбавленный в Дизельном масле до 5% Д.Д.Т. для ручного обрызгивания наружных помещений.

Население оказывало полное содействие, так как оно не только освобождалось от комаров, но одновременно и от других назойливых домашних насекомых. Это последнее обстоятельство чрезвычайно важно в подобных кампаниях.

Результаты показали резкое падение заболеваний малярией во время сезона, исчисляемых количеством паразитов, количеством заболевших детей и селезеночным указателем. Было произведено наблюдение над некоторыми недезинфицированными деревнями и при этом установлено, что 1946 год не был годом естественно низкого количества заболеваний в Греции. Греческое правительство без всякого колебания решило применить те же способы в 1947-ом году, как и в 1946-ом.

Главные заключения: 1. Необходимость иметь полные данные до того как составлять план работ. Проблемы малярии различны в разных странах и в различных частях той же самой страны.

2. Необходимость точного составления планов и полного сотрудничества со стороны

центрального и местного правительства, малириологов, санитарных инженеров и инспекторов, продовольственных, транспортных и финансовых чиновников, а главное всего местного населения.

3. Действие должно быть планомерным и вполне совпадать с привычками комаров.

4. Весьма важны информационные листки для населения и пропаганда посредством печати и радио.

5. В конце сезона рекомендуется особенно заняться теми местами, где разводятся комары. для того, чтобы уничтожить зимующих жироносных насекомых.

6. Требуется дальнейшее исследование других видов Д.Д.Т., для выяснения наилучших способов приготовления эмульсий, определения наилучшего пара-об'ема технических степеней, а также для определения эффекта длительной жары на хранение и выбор прочнейшего материала для сосудов.

7. Нужно выяснить точный ответ на следующие вопросы: а/ "Какие количества и концентрации Д.Д.Т. влияют на анофелесса в данном районе", и б/ "Какой срок эффективного действия Д.Д.Т. в различных концентрациях можно считать 100% успешным для известных площадей намеченных для обрызгивания".

8. Нужно еще много экспериментальной, технической и энтомологической работы для установления наиболее удовлетворительного и экономичного применения Д.Д.Т. в борьбе против малярии.

9. Насколько важно производить обрызгивание домов для уничтожения как комаров, так и их личинок, можно выяснить только при учете местных условий и в результате местных опытов в продолжении нескольких сезонов.

10. Токсический эффект Д.Д.Т. на людей до того ничтожен, что о нем не стоит и упоминать. Нужно только принимать меры предосторожности против инфекции кожи от действия керосина и масла, употребляемых вместе с Д.Д.Т. Этот вывод основан на наблюдении 6.000 рабочих, занятых за шесть летних месяцев.

SINCE 1935 sufficient information about malaria in Greece has been available for the practical purpose of planning schemes of control. Much work was done before then by Greek physicians and by a team sent by the Rockefeller Foundation in 1932. By 1945 more experience had been gained of control measures such as chemical and biological larvicides, nets and house screening, repellents and sprays of the "Flit" type, drainage schemes and suppressive drugs. In the civilian population these measures had had a degree of success in suitable areas (Table I), and in the British Army in Greece in 1945-46 the malaria rate was kept low by the controlled use of mepacrine, nets, dress regulations and larvicidal measures. However, the lack of discipline and co-operation in the civilian population and the shortage of labour and finance in 1945 gave little hope of success in an attempt to apply these measures or a combination of some of them on a national scale.

TABLE I.

Malaria Indices, School Age, Babyhood, 1945, 1946, *in Sprayed Villages of Sperchios, Argos, Nemea (Livadas).*

Village population	Date of		Spleen index			Para. index		Baby para. index	
	Spray	Index taking	No. Exd.	%	Av. Spl.	No. Exd.	%	No. Exd.	%
Kastri Paliouri 390	July '45	Autumn '45	48	48	0·90	48	4·2	—	—
	May '46	Autumn '46	73	25	0·30	74	2·7	10	0
Zilefton 345	July '45	Autumn '45	59	27	0·41	59	8·5	—	—
	May '46	Autumn '46	51	22	0·27	51	8·0	6	0
Myli 350	Aug. '45	Autumn '45	25	52	0·88	25	25	—	—
	May '46	Autumn '46	40	33	0·33	40	13	5	0
Galatas 235	Oct. '45	Autumn '45	34	82	1·53	27	26	—	—
	May '46	Autumn '46	48	85	1·33	48	17	9	0
Aedonia 385	Oct. '45	Autumn '45	50	88	1·72	43	30	—	—
	May '46	Autumn '46	68	65	0·88	68	4·4	11	0
Petri 242	Oct. '45	Autumn '45	29	89	1·45	20	15	—	—
	May '46	Autumn '46	59	41	0·56	59	6·8	12	0
Nea Kios 1900	Aug. '45	Autumn '45	79	44	0·51	43	2·3	24	0
	Apr. '46	Autumn '46	100	18	0·18	100	0	46	0
Malaria Indices, School Age, Babyhood, 1945, 1946, *in Unsprayed Village Rodonia (Sperchios)*									
Rodonia 428	—	Autumn '45	53	54	—	55	24	—	—
	—	Autumn '46	53	66	—	54	33	11	9

By 1945 the value of DDT as an insecticide and particularly in malaria control had been demonstrated by experiments in the U.S.A. The Sanitation Section of UNRRA Greece Mission under the direction of Colonel D. E. Wright, who had worked with the Rockefeller Foundation since Panama days and had been engaged in antimalarial work in Greece off and on since 1930, devised a plan for a nation-wide assault on both adult and larval anophelines using DDT in various forms as their sole weapon.

Briefly the plan was to use DDT wherever there was evidence of the presence of anophelines in an attempt at eradication. Four phases of operation were planned. The first was to handspray the interiors and overhanging portions of all buildings, houses, outhouses, stables, in fact any kind of erection or ruin where the hibernating insect might be found. Secondly, this spraying was to be repeated during the summer at intervals when the presence of not only mosquitoes but also common house-flies showed that there were parts omitted or that the DDT had lost its killing power.. Thirdly, on the first sign that surviving anophelines had emerged and were breeding, or on the generally accepted date when this was known to occur, to handspray every pool, watercourse, drain and swamp accessible to and capable of being effectively covered by this method. Control was to be maintained by dipping for larvæ and the spraying repeated at more or less regular intervals. Experimentally it appears that DDT spray is not affected by rainfall on water surfaces, and we did not automatically repeat spray for this reason. Fourthly, at the same time as the larvicidal attack by hand, we brought the aeroplanes into service over the more inaccessible swamps, lakes and water courses, under the same controls as by handspray.

UNRRA, backed by the opinion of eminent U.S. malariologists, was confident that malaria could be controlled by DDT alone. Greek malariologists, following experimental work with DDT, had no doubts as to its potentialities when used for house-spraying but they were not convinced that malaria could be eradicated from their country in one or two years. They maintain the same view to-day and reserve judgment on the widespread use of aeroplanes for spraying. UNRRA offered to provide skilled technical direction and to supply gratis the necessary DDT, oil, other materials, sprays, pumps, and a large fleet of trucks and motor cycles. UNRRA also offered to furnish the aeroplanes with a flying instructor and chief mechanic for their maintenance. By these offers and by Wright's enthusiasm the Greek Government was persuaded to vote large sums for the operation of the scheme.

THE PLAN IN ACTION

A trial of the ground methods was made in 1945 during the summer and autumn. This was more a period of training and organization than an operation, but where we worked the results in the fall in malaria incidence and in the eradication of other insect pests were so satisfactory that the Greek Government agreed from its straitened finances to increase the subsidy of £62,500 for 1945 to £300,000 for the major onslaught in 1946.

The organization set up was based on UNRRA HQ Athens and the Malariological Division of the Greek School of Hygiene, together with the Ministry of Hygiene. In each of eleven regions into which Greece had been divided under the British Military Government there were a Greek malariologist, an American Sanitary Engineer of the U.S.P.H.S., Greek Sanitary Engineers, and Greek inspectors and foremen trained in the technique of preparing the mixtures and spraying. These in their turn hired gangs of labourers and trained them to do the actual work. The Greek staff were paid by the malariologist acting as the Government agent. The scheme was directed and controlled in its major aspects from Athens.

During the winter of 1945-46 work commenced on the eradication of hibernators. For this a 5% mix of DDT in either kerosene or Diesel oil was used. Hudson sprayers delivered a heavy dose of 220 mg. DDT powder per sq. foot. As might be expected in a country so politically and economically disturbed as Greece was then and for that matter still is, there were many troubles both of operation and of supply, but at least the work had commenced and the machine was under way. At this time, too, clinical surveys were commenced both by the U.S.N. Epidemiological teams in Crete, Epirus and in the Peloponnesus, and by the Wellcome Research Foundation team, Foy and Kondi, working out of Salonica. The spleen and parasite findings of these surveys were to be compared with similar findings at the end of the year.

In the month of April attention was turned to the larvicidal work proper. Using DDT 5% in Diesel oil the well-established technique of spraying water accumulations up to about 5 kilometres from the outskirts of villages and hamlets was followed. Inspectors made frequent dippings for control. This continued throughout the summer and was terminated on September 30, which coincided with the early onset of cold weather. For political reasons a considerable disorganization of labour took place at this time and the return to the attack on possible hibernators was not as thorough as was planned.

We sprayed about 700,000 houses and outbuildings to November 1, using DDT prepared in four different ways as follows:

(1) DDT in kerosene using 7 oz. DDT to one gallon kerosene, approximately a 5% solution. The cost of this delivered to the villages was about two shillings per gallon. It

was used on the interior of houses only. An effort was made to give a uniform coat on the surface of 200 mg. per sq. foot.

(2) DDT 26% emulsion. This was received ready prepared in drums. We diluted it with five parts of water to one part of the emulsion and used it for the interiors of houses, beds and furniture. It does not stain and gives results as good as or better than pure DDT in kerosene. For larva control we diluted it to as much as eight parts of water with good results and a reduced price. The cost of the mix delivered and diluted five times was about one shilling and ninepence per gallon.

(3) DDT pure in Diesel oil as for kerosene. This was used for outbuildings, stables, sheepsheds, poultry houses and any other possible resting places for mosquitoes. The cost was about one shilling and ninepence per gallon.

(4) DDT 20% in Velsicol (Velsicol NR 70, polymethyl naphthalene, good solvent, high boiling range and flash point) was used for all aeroplane work without further dilution, but it also gave excellent results for outbuildings by diluting five gallons of Diesel oil to one gallon of the mix. It causes a heavy stain but its lasting qualities are excellent and give protection for as long as six months with one application. There is also a 35% emulsion available, an advantage where the portage of a quantity by a labourer is a problem.

Aeroplanes were intended to play a role secondary to the ground methods but as the work went on we found more and more uses for air-spraying. The Press dramatized the flying part of the programme and we had difficulty in persuading the Greeks that we had no ideas of ridding them of malaria by flying-machines. Eighteen small training planes of the U.S.A.A.F. Stearman type were used. They are single-motored with a cruising speed of about 90 m.p.h. and a landing speed of 40 m.p.h. They were flown by Royal Hellenic Air Force pilots specially trained in the flying technique and given some instruction in malariology. Ten principal bases and many subsidiary landing strips were used. The pilot made a preliminary ground and air survey of his section with the local malariologist or sanitary engineer and then sprayed it when the air was calm from a minimum height of 10 feet. The density of the mist was controlled by a Venturi jet and could be estimated by an observer on the ground. The swamps of Greece lend themselves to this type of spraying. There are few if any trees and the aquatic vegetation is light. Also, during the spring and summer one can count upon fine weather. In 1946 there was no rain to speak of and the long period of drought aided us by shrinking the size of many shallow lakes and swamps. The area which we considered on the basis of larva surveys should be sprayed was 113,000 acres at the beginning of the season and by the end had shrunk to 80,000 acres.

Under ordinary conditions the pilots could spray about 17 acres per minute, but on the basis of the total flying time, including the flight to and from the base, the speed worked out at 4 acres per minute. In all, 506,356 acres were sprayed which represented a 5·3 times spraying of the average number of acres (96,000) sprayed during the season. The total cost, excluding the initial cost of the planes (£6,000) but including pilots, mechanics, labourers and watchmen, was £20,460 or 4s. 4½d. per acre.

A comparison of the cost and man-power required for the various methods of spraying is given in Table II.

TABLE II.—SHOWING CERTAIN FIGURES OF SPRAYING CAPACITY, MAN-POWER POTENTIAL, AND COSTS, WHEN USING VARIOUS METHODS AND MATERIALS FOR SPRAYING IN MALARIA CONTROL.

	Oil	Paris Green dust	Paris Green suspension	DDT planes	DDT hand Oil	DDT hand Emulsion
(1) 1,000 sq. metres requires	35 Lit.	0·2 Lit.	0·09 Lit. dust	0·012 kg. DDT 100% in Velsicol 51·0 c.c.	0·010 kg. 100% as 5%	0·012 kg. 100% as 1%
(2) One man can cover daily	1,200 sq. metres	3,700 sq. metres	3,500 sq. metres	1,100,000 sq. metres per one flying hour*		
(3) He uses for this	42 Lit.	74 Lit.	210 Lit.	56 Lit. for 1 hr. flight*	0·25 Lit. 5% per 1,000 sq. metres	1·25 Lit. 1% DDT per 1,000 sq. metres
(4) Approx. cost of treating 10,000 sq. metres	$18§ £4 10s.	$3.80§ 19s.	$2.20§ 11s. (80% larva kill)	40 cents† 2s.	$3.60‡ 18s.	$3.60 18s.

*The actual spraying time was about one-fourth total flying time.
†In proportion of two for material and one for labour (Greece, 1946).
‡In proportion of about one for material and thirteen for labour.
§Pre-war prices.
NOTE.—Cost of transport and general expenses is not included.

In fairness to the plan it has to be recorded that there were many difficulties in the use of Government-hired labour and in securing delivery of supplies to schedule. Political and administrative moves frequently threatened to break the scheme and succeeded in causing irritation and delays.

SIDE-EFFECTS OF DDT SPRAYING

In Athens in 1946, the most surprising thing was an almost entire absence of flies. In addition to the use of DDT in private houses, large garbage dumps on the end of the town were sprayed from the air at intervals during the hot weather. Air-spraying appeared to clear sandflies from the Nea Smyrna suburb of Athens. It was successfully used against the Dacus fly in olive groves and against a plague of Tene moth in pine and fruit trees. In the interests of the beekeepers care was taken not to use DDT where bees drew their sustenance.

The notifications of typhoid and dysentery in the whole of Greece (Table III) although probably not very accurate do suggest that the reduction of flies by spraying from about July onwards affected the dysentery figures. Typhoid in Greece is mainly a matter of water supply and one would not expect similar results from the eradication of flies.

TABLE III.—NOTIFICATIONS OF TYPHOID AND DYSENTERY FOR ALL GREECE

	1945		1946	
	Typhoid	Dysentery	Typhoid	Dysentery
May	130	12	96	69
June	338	135	215	62
July	434	268	520	151
August	803	581	498	85
September ..	727	500	340	12
October	396	152	221	6

EFFECT OF DDT SPRAYING ON MALARIA

Damkas and Mandekos, Rockefeller-trained malariologists who worked in Macedonia with UNRRA and the Government respectively, have supplied figures of spleen indices for a large number of places. The 1946 figures showed a consistent fall below the 1945 level and usually below any level recorded in previous years. In 13 places where no such fall was found, investigations showed that DDT residual spraying was not done (3 places), was delayed or partial (7 places) or that the technique was bad (3 places). Parasite indices in a number of places also showed a fall, but the full results will not be available for some time. Livadas and his co-workers examined in 7 villages 99 babies born after the end of the 1945 season. They were all negative for plasmodia at the end of the 1946 season. In a control non-sprayed village 1 of 11 babies was positive.

In judging the effect of the DDT campaign it is of the greatest importance to establish whether 1946 was naturally a year of low endemicity or not. There are differences of opinion on this. Livadas with his great experience of malaria control in his native land sums up as follows:

> "1946 was preceded by three years, 1943, 1944 and 1945, of comparatively high drought during which malaria remained, after the high level of 1942, at more or less low levels. The abundant rainfall of late 1945 and early 1946 created favourable hydrological conditions for anopheline breeding. It was noted that the early generations of anophelines in 1946 were more numerous than usual, and there was agreement among the experts that there would follow an increased endemicity as is usually the case in Greece every three to five years.
>
> "The ensuing drought, relatively low temperature of the summer and the steady trade winds led to the conclusion that even where no malaria control was carried out the early pessimistic views might be discounted.
>
> "However, actual investigation showed that the anopheline density was not lower than in years of average endemicity. For example, Rodonia village, unprotected from malaria, showed aside from a clear rise of malaria indices a typical local rise in parasite indices, all carriers showing *P. falciparum*. It is also noted that mosquito density in that region approached proportions of epidemic years . . . It is not right to generalize from the above observations, but the conclusions from the evidence to date may be given as follows:
>
> "(i) The level of malaria endemicity in 1946 varied substantially from area to area as is usual in Greece.
>
> "(ii) The assumption is well justified that if the epidemiological conditions of 1946 proved on the whole less favourable for the development of malaria compared with 1938 and 1942 (the more recent epidemic years in Greece) yet they were undoubtedly more favourable than the conditions prevalent during the immediately preceding years of 1943, 1944 and 1945.
>
> "This being so, the surprising improvement of the malaria condition noted in 1946 must be attributed in a very great measure to the malaria control programme, and more particularly to the extensive use of the DDT house-spray technique."

It must be mentioned that atebrin was supplied by UNRRA and distributed in large quantities through local M.O.sH. and Malaria Control Officers during the winter of 1945-46. It is thought that there was not much use of the drug though there is no good evidence either way. It is possible that the availability of atebrin to some extent masked the value of the DDT spraying. Among the UNRRA 2,000 or so personnel atebrin was issued in the spring of 1946 with a recommendation as to its use. The usual story is that some of them took it for a few weeks and then gave it up as there did not seem to be any mosquitoes; similarly with nets, which were hardly used at all. In fact we have travelled over the whole of Greece and lived in provincial small towns without being conscious of a mosquito problem. There have been no new cases of malaria amongst UNRRA personnel.

Further evidence of the success of the campaign was gained from returns by Greek Regional Health Centres when asked by the School of Hygiene for information on malaria incidence during 1946. Eleven centres described the incidence as "reduced", seven as "considerably reduced", nine as "very low", six as "surprisingly low" and four as "practically non-existent". It was noteworthy that the fall in morbidity corresponded with the extent of the campaign in each prefecture. Four health centres reported a small epidemic incidence in non-protected areas and all others no local epidemic incidence whatever. Information from hospitals showed generally a satisfactory fall in numbers of patients treated. It will require a further year or two of intensive effort before the reduction in malaria will be noticeable among the population in general.

Livadas and the School of Hygiene estimate that some 3,600,000 persons were protected; that is about 80% of the total population at risk. The cost per capita was 2s., i.e. the present price of two tablets of quinine, or very much less than one-fifth of the cost of a single intramuscular injection by a private doctor. The total proposed as the budget for 1947 is, however, in the region of £300,000 and it is a very real problem to produce it. The aeroplanes and the DDT have been UNRRA gifts, as have most of the transport vehicles which after a season on the roads of Greece are not in such good shape as they were. The biggest expense is the hire of labour for spraying, and it is the opinion of many of us that this work can be carried out by voluntary or locally paid labour in the villages themselves without drawing on central Government funds. A staff of peripatetic inspectors could instruct and supervise.

It will be interesting to follow the 1947 effort. On the credit side there is the experience gained in 1946 both in headquarters and among the ranks in the field. There is ample DDT of all kinds in Greece now, whereas last year we did not get enough until well on into the summer. Against this, we start with the country in a terribly disturbed condition. Many key men, professional and technical, have been discharged for political reasons. There is a pitiful number of malariologists available, a hopelessly inadequate force. Transport is a greater problem than last year and may well modify the whole plan. There are only two as against seven or eight imported engineers for help and supervision and the essential reliable reporting service. There is, however, one advantage which must be mentioned. Amongst the people of Greece of all classes there are now no sceptics as to the value of this method of fighting malaria and dealing with other insect pests.

We feel that a vigorous effort must be made this year and perhaps for one or two more seasons. After that we think that a careful watch by the Malaria Service of the School of Hygiene and a relatively small action group on an insignificant budget should be sufficient to control this plague, always assuming that there will be something of a continual effort by the population itself to use DDT for the other reasons stressed in this paper. The mosquito will not be eradicated in Greece. While there are anopheles and the odd carrier of malaria there will always be the danger, as in other countries not excepting parts of England. But that it is capable of control to relative unimportance we think is well within the realms of possibility.

I should like to pay tribute to the services of Professor Gregory Livadas and the staff of the Athens School of Hygiene for their work and their co-operation in this campaign. They carried a great burden in organization and their enthusiasm and energy were maintained throughout the season, under the most difficult conditions, both political and economic. I should also like to thank Colonel D. E. Wright, Rockefeller Foundation and during 1946 Chief Sanitary Engineer of the UNRRA Greece Mission, for the great work he carried out, for the keenness and energy he brought to the problem, and for the willing assistance he gave me in the preparation of this paper.

ADDENDUM.—During the months which have elapsed between the presentation of Dr. Vine's paper and its publication further data and conclusions from the 1946 Campaign became available and Dr. Vine, writing from Athens in October 1947, requested us to add the following observations which bear upon the material of his original paper. More mature

considerations of the operation in 1946 have led to certain conclusions and principles, some of which have been incorporated into the 1947 Campaign:

(1) The supreme importance of available and up-to-date complete data with regard to the biological, sociological, geographical, meteorological and entomological conditions of the areas to be dealt with, before the operation is planned. The above were all available to us but the War and Occupation had, to some extent, limited continuous clinical observations.

(2) The almost equal importance of establishing full understanding and co-operation between all sections engaged in the operation. This means both central and local government, malariologists, sanitary engineers and inspectors, supply and transport staff, finance officers and finally, and very important, the local population. The Campaign must be planned on the lines of a military operation with the complication of the civilian element in the forefront. Our own plans were worked out on such lines and we had full co-operation.

(3) In connexion with the above, the public must know what is going on and must be advised by leaflets and through the popular press and wireless broadcasts. We used all the above methods with satisfactory results.

(4) The timing of the different phases subject to anopheline habits presents problems in organization. Thus in Greece, *A. superpictus* can be overlooked until June-July, whereas *A. elutus* and *A. maculipennis* must be attacked in April.

(5) If at all possible, bloods, spleens and baby rates should be investigated over typical "bad" malaria areas, both before and immediately after the season. Baby rates are of a special value and we have much valuable information from this in certain areas, especially Northern Greece.

(6) It is advantageous to make a final onslaught on known breeding sites, particularly marshes, at the end of the season, with the object of diminishing the number of potential fat-bearing hibernators.

(7) With regard to bees, we found that where DDT is used after blossom time there was little or no mortality and this observation compares favourably with the mortality from other forms of insect control drugs on fruit, and vegetables, e.g. arsenic in molasses. On the other hand, we confirm that DDT used in a house where silkworms are breeding inevitably causes death of the worms. Draughts and vibration free the crystals from the sprayed surfaces and these are carried to other parts of the house.

(8) In our experience of 6,000 labourers over a period of six summer months, the toxic effect of DDT on humans is negligible. The effect, however, of kerosene and oil on the skin has to be considered and the appropriate precautions put into force.

We also suggest that in the use of DDT there are several important "unknowns" amongst which are the following:

(*a*) The full answers to the questions: "How does DDT in the area quantities and concentrations used affect the adult anopheline?" and "What is the contact-time element of 100% effectiveness of different concentrations per area of DDT residual spraying?"

(*b*) What are the relative values of larvicidal methods as against house spraying and as against a combination of both? The answer depends, of course, on local conditions but it has to be found for each campaign. In Greece we favour a combination of both and ideally we would propose completion of the first house-spraying before the first brood of larvæ develops.

(*c*) We believe there is room for further investigation by manufacturers as to the most effective agents in preparing emulsions of DDT. There are also problems of the optimum *para-para* content of technical grades of DDT. Similarly the effect of prolonged atmospheric heat and bad storage and the optimum container material for DDT are subjects, no doubt, under investigation, and requiring elucidation. Also, as DDT is readily saleable privately, care must be taken that solutions and emulsions made up in the field contain their ingredients in the proper amounts.

(*d*) Finally, it is clear that much experimental work, both technical and entomological, must be done before the most satisfactory and economic use of DDT in malaria control on the grand scale is determined.

Section of Laryngology with Section of Otology

COMBINED SUMMER MEETING HELD IN BRIGHTON

[*June* 27, 1947]

LARYNGOLOGICAL SESSION

Chairman—NORMAN PATTERSON
(President of the Section of Laryngology)

Certain Anatomical and Physiological Considerations in Paralysis of the Larynx

By V. E. NEGUS

THERE is considerable confusion in descriptions of laryngeal paralysis, and this confusion seems to arise from different causes. The first difference of opinion concerns the nerve supply of the laryngeal muscles, the second their mode of action, and the third the appearances and description of the results of disturbances of innervation. It will be best, therefore, to discuss the question under various headings.

Nerve supply.—I have obtained from Dr. G. Weddell the correct interpretation of the derivation of the motor fibres supplying the intrinsic muscles of the larynx; it is stated that they are localized in the lower part of the nucleus ambiguus, which belongs to the spinal accessory nerve [1]. The fibres arising from these motor cells leave the cranium in the eleventh nerve, which then divides into an internal and external branch. The former joins the ganglion nodosum of the vagus nerve, in which the fibres travel to reach the larynx, either through the superior laryngeal branch or through the recurrent laryngeal nerve. There is no particular clinical significance in this observation, as lesions at the jugular foramen, such as a new growth, fracture or other injury, would, in all probability, involve both the tenth and eleventh nerves, and any lesion in the medulla of any wide extent would probably involve the motor nuclei of both the tenth and eleventh nerves. It is, however, best for the sake of accuracy to decide this point, and this seems to represent the modern opinion.

The second point concerns the supply of the intrinsic laryngeal muscles. It is agreed that the crico-arytenoideus posticus and the sphincteric group, made up of lateral crico-arytenoid and thyro-arytenoid muscles, together with the interarytenoid, are all supplied by the recurrent laryngeal nerve. The interarytenoid has, of course, a bilateral supply. What is in dispute is the function of the superior laryngeal, which through its external branch gives innervation to the crico-thyroid muscles. It has been thought by some that the interarytenoid was also supplied by this nerve, but this view, according to Lemere and others, is incorrect [2, 3]. It should be accepted that the superior laryngeal nerve supplies the crico-thyroid muscle only and the recurrent, the intrinsic abductor and adductor muscles.

considerations of the operation in 1946 have led to certain conclusions and principles, some of which have been incorporated into the 1947 Campaign:

(1) The supreme importance of available and up-to-date complete data with regard to the biological, sociological, geographical, meteorological and entomological conditions of the areas to be dealt with, before the operation is planned. The above were all available to us but the War and Occupation had, to some extent, limited continuous clinical observations.

(2) The almost equal importance of establishing full understanding and co-operation between all sections engaged in the operation. This means both central and local government, malariologists, sanitary engineers and inspectors, supply and transport staff, finance officers and finally, and very important, the local population. The Campaign must be planned on the lines of a military operation with the complication of the civilian element in the forefront. Our own plans were worked out on such lines and we had full co-operation.

(3) In connexion with the above, the public must know what is going on and must be advised by leaflets and through the popular press and wireless broadcasts. We used all the above methods with satisfactory results.

(4) The timing of the different phases subject to anopheline habits presents problems in organization. Thus in Greece, *A. superpictus* can be overlooked until June-July, whereas *A. elutus* and *A. maculipennis* must be attacked in April.

(5) If at all possible, bloods, spleens and baby rates should be investigated over typical "bad" malaria areas, both before and immediately after the season. Baby rates are of a special value and we have much valuable information from this in certain areas, especially Northern Greece.

(6) It is advantageous to make a final onslaught on known breeding sites, particularly marshes, at the end of the season, with the object of diminishing the number of potential fat-bearing hibernators.

(7) With regard to bees, we found that where DDT is used after blossom time there was little or no mortality and this observation compares favourably with the mortality from other forms of insect control drugs on fruit, and vegetables, e.g. arsenic in molasses. On the other hand, we confirm that DDT used in a house where silkworms are breeding inevitably causes death of the worms. Draughts and vibration free the crystals from the sprayed surfaces and these are carried to other parts of the house.

(8) In our experience of 6,000 labourers over a period of six summer months, the toxic effect of DDT on humans is negligible. The effect, however, of kerosene and oil on the skin has to be considered and the appropriate precautions put into force.

We also suggest that in the use of DDT there are several important "unknowns" amongst which are the following:

(*a*) The full answers to the questions: "How does DDT in the area quantities and concentrations used affect the adult anopheline?" and "What is the contact-time element of 100% effectiveness of different concentrations per area of DDT residual spraying?"

(*b*) What are the relative values of larvicidal methods as against house spraying and as against a combination of both? The answer depends, of course, on local conditions but it has to be found for each campaign. In Greece we favour a combination of both and ideally we would propose completion of the first house-spraying before the first brood of larvæ develops.

(*c*) We believe there is room for further investigation by manufacturers as to the most effective agents in preparing emulsions of DDT. There are also problems of the optimum *para-para* content of technical grades of DDT. Similarly the effect of prolonged atmospheric heat and bad storage and the optimum container material for DDT are subjects, no doubt, under investigation, and requiring elucidation. Also, as DDT is readily saleable privately, care must be taken that solutions and emulsions made up in the field contain their ingredients in the proper amounts.

(*d*) Finally, it is clear that much experimental work, both technical and entomological, must be done before the most satisfactory and economic use of DDT in malaria control on the grand scale is determined.

Section of Laryngology with Section of Otology

COMBINED SUMMER MEETING HELD IN BRIGHTON

[*June* 27, 1947]

LARYNGOLOGICAL SESSION

Chairman—NORMAN PATTERSON
(President of the Section of Laryngology)

Certain Anatomical and Physiological Considerations in Paralysis of the Larynx

By V. E. NEGUS

THERE is considerable confusion in descriptions of laryngeal paralysis, and this confusion seems to arise from different causes. The first difference of opinion concerns the nerve supply of the laryngeal muscles, the second their mode of action, and the third the appearances and description of the results of disturbances of innervation. It will be best, therefore, to discuss the question under various headings.

Nerve supply.—I have obtained from Dr. G. Weddell the correct interpretation of the derivation of the motor fibres supplying the intrinsic muscles of the larynx; it is stated that they are localized in the lower part of the nucleus ambiguus, which belongs to the spinal accessory nerve [1]. The fibres arising from these motor cells leave the cranium in the eleventh nerve, which then divides into an internal and external branch. The former joins the ganglion nodosum of the vagus nerve, in which the fibres travel to reach the larynx, either through the superior laryngeal branch or through the recurrent laryngeal nerve. There is no particular clinical significance in this observation, as lesions at the jugular foramen, such as a new growth, fracture or other injury, would, in all probability, involve both the tenth and eleventh nerves, and any lesion in the medulla of any wide extent would probably involve the motor nuclei of both the tenth and eleventh nerves. It is, however, best for the sake of accuracy to decide this point, and this seems to represent the modern opinion.

The second point concerns the supply of the intrinsic laryngeal muscles. It is agreed that the crico-arytenoideus posticus and the sphincteric group, made up of lateral crico-arytenoid and thyro-arytenoid muscles, together with the interarytenoid, are all supplied by the recurrent laryngeal nerve. The interarytenoid has, of course, a bilateral supply. What is in dispute is the function of the superior laryngeal, which through its external branch gives innervation to the crico-thyroid muscles. It has been thought by some that the interarytenoid was also supplied by this nerve, but this view, according to Lemere and others, is incorrect [2, 3]. It should be accepted that the superior laryngeal nerve supplies the crico-thyroid muscle only and the recurrent, the intrinsic abductor and adductor muscles.

considerations of the operation in 1946 have led to certain conclusions and principles, some of which have been incorporated into the 1947 Campaign:

(1) The supreme importance of available and up-to-date complete data with regard to the biological, sociological, geographical, meteorological and entomological conditions of the areas to be dealt with, before the operation is planned. The above were all available to us but the War and Occupation had, to some extent, limited continuous clinical observations.

(2) The almost equal importance of establishing full understanding and co-operation between all sections engaged in the operation. This means both central and local government, malariologists, sanitary engineers and inspectors, supply and transport staff, finance officers and finally, and very important, the local population. The Campaign must be planned on the lines of a military operation with the complication of the civilian element in the forefront. Our own plans were worked out on such lines and we had full co-operation.

(3) In connexion with the above, the public must know what is going on and must be advised by leaflets and through the popular press and wireless broadcasts. We used all the above methods with satisfactory results.

(4) The timing of the different phases subject to anopheline habits presents problems in organization. Thus in Greece, *A. superpictus* can be overlooked until June-July, whereas *A. elutus* and *A. maculipennis* must be attacked in April.

(5) If at all possible, bloods, spleens and baby rates should be investigated over typical "bad" malaria areas, both before and immediately after the season. Baby rates are of a special value and we have much valuable information from this in certain areas, especially Northern Greece.

(6) It is advantageous to make a final onslaught on known breeding sites, particularly marshes, at the end of the season, with the object of diminishing the number of potential fat-bearing hibernators.

(7) With regard to bees, we found that where DDT is used after blossom time there was little or no mortality and this observation compares favourably with the mortality from other forms of insect control drugs on fruit, and vegetables, e.g. arsenic in molasses. On the other hand, we confirm that DDT used in a house where silkworms are breeding inevitably causes death of the worms. Draughts and vibration free the crystals from the sprayed surfaces and these are carried to other parts of the house.

(8) In our experience of 6,000 labourers over a period of six summer months, the toxic effect of DDT on humans is negligible. The effect, however, of kerosene and oil on the skin has to be considered and the appropriate precautions put into force.

We also suggest that in the use of DDT there are several important "unknowns" amongst which are the following:

(*a*) The full answers to the questions: "How does DDT in the area quantities and concentrations used affect the adult anopheline?" and "What is the contact-time element of 100% effectiveness of different concentrations per area of DDT residual spraying?"

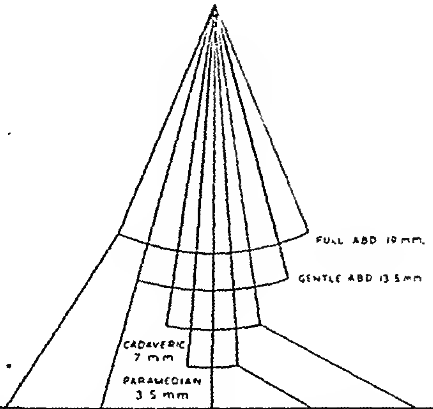
(*b*) What are the relative values of larvicidal methods as against house spraying and as against a combination of both? The answer depends, of course, on local conditions but it has to be found for each campaign. In Greece we favour a combination of both and ideally we would propose completion of the first house-spraying before the first brood of larvæ develops.

(*c*) We believe there is room for further investigation by manufacturers as to the most effective agents in preparing emulsions of DDT. There are also problems of the optimum *para-para* content of technical grades of DDT. Similarly the effect of prolonged atmospheric heat and bad storage and the optimum container material for DDT are subjects, no doubt, under investigation, and requiring elucidation. Also, as DDT is readily saleable privately, care must be taken that solutions and emulsions made up in the field contain their ingredients in the proper amounts.

(*d*) Finally, it is clear that much experimental work, both technical and entomological, must be done before the most satisfactory and economic use of DDT in malaria control on the grand scale is determined.

lengthened, and the Wrisberg cartilage may lie further back than on the unaffected side. In the aryepiglottic fold there are, on the outer side of the Wrisberg cartilage, muscular fibres continuous with the interarytenoid which have an active function in closing the aperture of the larynx during swallowing. It is common to find, therefore, that in recurrent laryngeal paralysis, with a partial loss of the protective action of the aryepiglottic folds, liquids tend to overflow into the larynx, as in the case of bulbar paralysis, thus causing considerable coughing and distress to the patient.

Positions of the vocal cords.—There has been in the past some confusion in describing the positions of the vocal cords, and it would be well to reach agreement as to nomenclature. An excellent paper by Clerf and Suehs is of particular value in clarifying this problem [3]. There are six positions to be described (fig. 1).



POSITION	FULL ABDUCTION	GENTLE ABDUCTION	MEDIAN	PARAMEDIAN	INTERMEDIATE
FUNCTION	DEEP INSPIRATION	QUIET RESPIRATION	PHONATION	STRONG WHISPER	CADAVERIC
ACTIVE MUSCLES	ALL	ABDUCTORS	ADDUCTORS	EXTERNAL ADDUCTORS	NONE
SOMETIMES PARALYSED	NONE	INTERNAL ADDUCTORS	ABDUCTORS	INTERNAL ADDUCTORS	ALL

FIG. 1.—Diagram to illustrate positions assumed by the vocal cords in health and disease. In addition to the five illustrated, a sixth, the "glottic chink," is assumed in some cases of double abductor paralysis.

Starting at the middle, there is the *median* position, which is adopted during phonation, under the action of the external and internal adductors. The median position can be taken up in cases of paralysis of the abductors when, according to Semon's law, the latter alone are paralysed.

The second position may be known as the abductor or *glottic chink*; it appears in cases of double abductor paralysis. Although, in this condition, the external and internal adductors bring the cords together, the lack of bracing back of the arytenoid cartilages by the posticus muscles allows the margins of the cords to separate very slightly during inspiration and more still during expiration [4]. If there were not this chink, the patient would be asphyxiated, and in point of fact he may be near this condition in certain early cases of double abductor paralysis.

The third position is the *paramedian* [2, 3], which leaves a posterior space of about 3·5 mm. between the cords. It is the position used in certain forms of strong whisper, and in pathological states it is taken up in cases of complete paralysis of the recurrent laryngeal nerve, when both the abductors and the internal adductor muscles are out of action. The cords are brought into the paramedian position by the influence of the crico-thyroid muscles, which act as external adductors and rotators of the arytenoid cartilages, and thus as tensors of the vocal cords [2, 3, 5]. It is incorrect to say that in cases of complete recurrent paralysis the cadaveric position is taken up.

The fourth position is the *cadaveric*, in which the posterior arm of the glottic triangle measures about 7 mm. It is the position of complete muscular relaxation and is assumed by virtue of the elasticity of the capsule forming the crico-arytenoid joint. It is only assumed when all the muscles controlling the glottic margins are paralysed, that is, the internal and

Action of intrinsic laryngeal muscles.—In considering paralysis of the larynx, the function of the *crico-thyroid muscle* is of considerable importance. By narrowing the gap between the cricoid and thyroid cartilages and by sliding the thyroid forward in relation to the cricoid, the distance between the crico-arytenoid joint and the inner surface of the thyroid alæ is lengthened. This means that the crico-thyroid in its contraction is an external tensor of the vocal cords. The same action has a rotatory effect which tends to bring the vocal processes of the arytenoids closer to one another. It should therefore be agreed that the crico-thyroid muscles act as external tensors and adductors of the vocal cords. As to which moves on the other, cricoid on thyroid, or vice versa, there is also disagreement. I believe the correct explanation is that during phonation the cricoid cartilage is held immovably against the front of the vertebral column by the action of the crico-pharyngeal sphincter and that when the crico-thyroid muscles contract, they rotate the thyroid on the stationary cricoid. During swallowing, on the other hand, the crico-pharyngeus relaxes and allows the cricoid cartilage to be tilted forward during closure of the laryngeal aperture. These are minor points, but of some interest.

The second observation, in the interest of clarity, concerns the action of the *crico-arytenoideus posticus*. The action of this muscle is of two types. In the first place the posterior fibres, attached to the muscular process of the arytenoid, rotate the latter and separate the vocal or glottic processes of the cartilages. In the second place, there are lateral fibres of the posticus muscle arising from the outer surface of the cricoid cartilage, to gain attachment to the body of the arytenoid; they slide the whole of the latter outwards on its lax joint, thus separating the bodies of the arytenoids. By this dual action, the posticus muscle opens the glottis, making it of a triangular shape, but if the usual description were correct, and rotation by traction on the muscular processes were the only action, then the glottis would be diamond-shaped when open.

Another action of the posticus muscle is to brace back the arytenoid cartilage during phonation. If this were not so, contraction of the sphincteric group of muscles would pull the arytenoid forward and there would be no possibility of obtaining tension in the margins of the glottis. As it is, the counteraction of the posticus allows the thyro-arytenoid muscles to provide elasticity to the glottic margins, the degree of elasticity varying with the pitch required, becoming greater as the pitch rises. During raising of the pitch, the increasing tension of the thyro-arytenoid muscles tends to shorten the vocal cords, a point disputed by some.

In a case of partial recurrent laryngeal paralysis, where the abductor muscle alone is paralysed, the arytenoid cartilage is allowed to slide forwards and inwards and will therefore approach the thyroid ala and will drop to a lower level. This action is increased if the internal adductors and tensors are still functioning. If there is, however, complete recurrent laryngeal paralysis, the forward and shortened position will still be taken up (fig. 2, diagrams 3 and 5). A fourth function of the posticus muscle will be considered later.

Control of the aryepiglottic fold.—It is a habit to speak of "paralysis of the cord", but in certain cases the cord itself is invisible, as it is overhung and obscured by the aryepiglottic fold. It is therefore necessary to consider the function of the latter. It is a fold designed to provide a lateral food channel, which leads down from the side of the epiglottis through the pyriform fossa to the mouth of the œsophagus. Small quantities of liquid are able to travel past the larynx even if the latter is open, and in herbivorous animals and in many Cetaceans the use of this lateral channel is the habitual manner of swallowing. In man, with his herbivorous ancestry, the fold is high, and use is made of it, particularly in infancy. The fold is attached anteriorly to the lateral border of the epiglottic cartilage and posteriorly to the body of the arytenoid and to the anterior surface of the cartilage of Santorini. The fold is kept more or less tense by the backward pull of the posticus muscle, which so braces it that it remains upstanding; but the upright position is also facilitated by the cartilage of Wrisberg, which acts as a passive prop. If the posticus muscle is paralysed, the arytenoid cartilage is no longer braced back, and the aryepiglottic fold falls forwards and inwards, overlying the laryngeal aperture. It is easy to see, in a case of recurrent laryngeal paralysis, this alteration in position of the aryepiglottic fold, which is particularly indicated by the falling forwards and inwards of the cartilage of Wrisberg. The latter lies in an anterior position in relation to its normal fellow of the opposite side. One can therefore see that there is an abductor, or a complete recurrent laryngeal paralysis, by observing the Wrisberg cartilage, even if the vocal cord is invisible. During phonation, the action of the internal tensors and adductors brings the vocal cord of the opposite side towards the mid-line and shortens it. In this action, the Wrisberg cartilage of the healthy side passes in front of that of the paralysed side (fig. 2, diagrams 3 and 5). This movement and difference of position is of considerable value in a differential diagnosis between paralytic and mechanical fixation of a vocal cord. In fact, when the crico-arytenoid joint is affected, the aryepiglottic fold appears

The points of importance suggested for consideration are the necessity for clear expression regarding the paramedian and cadaveric positions, and the differentiation between recurrent laryngeal paralysis and what I would suggest should be called combined paralysis, when both branches of the vagus are involved.

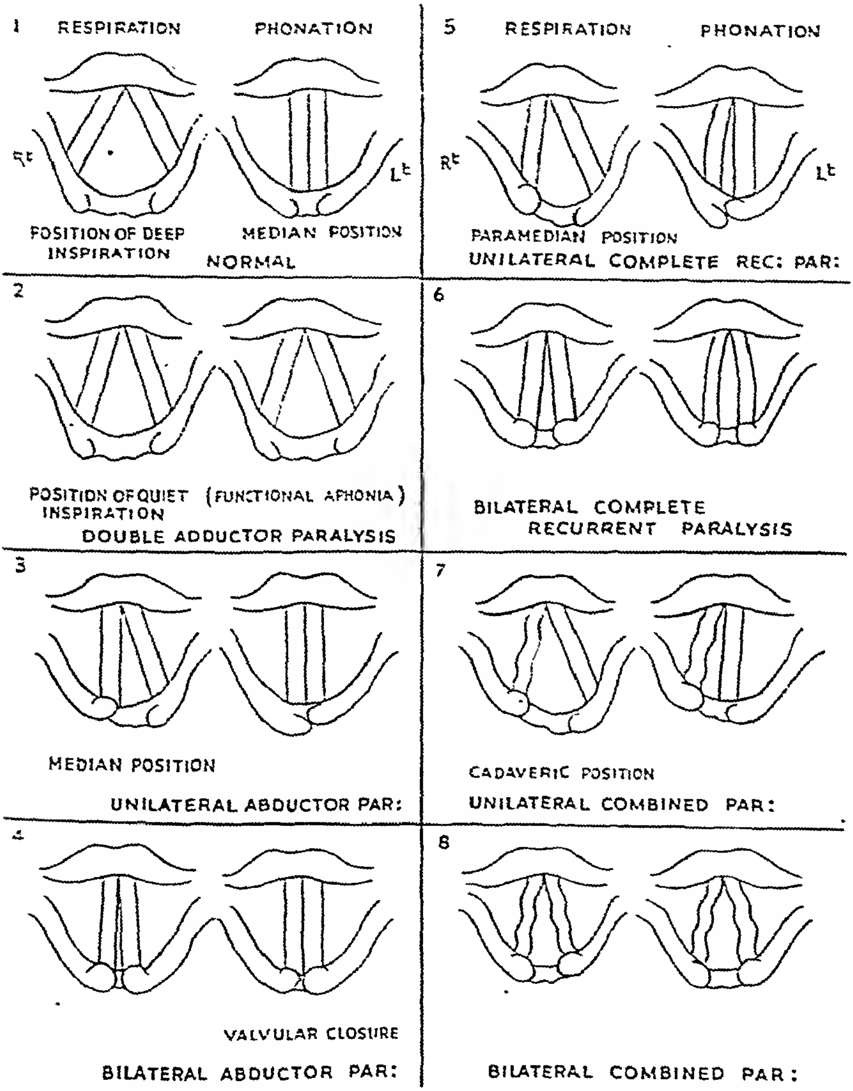

1
RESPIRATION
PHONATION
Rt
Lt
POSITION OF DEEP INSPIRATION
MEDIAN POSITION
NORMAL
5
RESPIRATION
PHONATION
Rt
Lt
PARAMEDIAN POSITION
UNILATERAL COMPLETE REC: PAR:
2
POSITION OF QUIET INSPIRATION
(FUNCTIONAL APHONIA)
DOUBLE ADDUCTOR PARALYSIS
6
BILATERAL COMPLETE RECURRENT PARALYSIS
3
MEDIAN POSITION
UNILATERAL ABDUCTOR PAR:
7
CADAVERIC POSITION
UNILATERAL COMBINED PAR:
4
VALVULAR CLOSURE
BILATERAL ABDUCTOR PAR:
8
BILATERAL COMBINED PAR:

FIG. 2.—Diagrams to illustrate the appearances of the larynx in paralytic conditions. In each, inspiration is represented on the left and phonation on the right. The overhanging position of the aryepiglottic fold and cartilage of Wrisberg is often more exaggerated than illustrated above.

(Figs. 1 and 2 appear in "Diseases of the Nose and Throat" by StClair Thomson and V. E. Negus, 5th Ed., and are reproduced by kind permission of the publishers, Messrs. Cassell & Co., Ltd., London.)

REFERENCES

1 WEDDELL, G. (1942) Personal Communication.
2 LEMERE, F. (1932) *Amer. J. Anat.*, 51, 417; (1933) *Arch. Otolaryng., Chicago*, 18, 413; (1934) *Ann. Otol. Rhin. Laryng.*, 43, 523.
3 CLERF, L. H., and SUEHS, O. W. (1941) *Ann. Otol. Rhin. Laryng.*, 50, 762.
4 LEDERER, F. L. (1943) Diseases of the Ear, Nose and Throat, Philadelphia, 4th Ed.
5 HOFER, G., and JESCHEK, J. (1940) *Z. f. Hals-Nas. u. Ohrenheilk.*, 45, 401.
6 COLLEDGE, L. (1935) Encycl. Brit. Med. Practice., Ed. Rolleston, H., London, 7, 612.

external adductors and the abductors. It can therefore only come about in cases of vagus paralysis, where both the superior laryngeal nerve and the recurrent nerve are out of action. It is not a position adopted in cases of recurrent laryngeal paralysis without involvement of the superior branch. The cadaveric is sometimes known as the *intermediate* position [3], as it lies roughly half-way between the mid-line and the fifth position of *quiet respiration.* The latter is the position of gentle abduction and is seen during peaceful respiration, the glottic space measuring about 13·5 mm. transversely. The cords are maintained in this position under the influence of the abductors. It is also the position assumed in functional aphonia, but not because of any organic paralysis. It could not, in fact, be assumed in any organic lesion, because it necessitates activity of the posticus muscle.

The sixth position is that of *full abduction*, assumed during deep respiration under the influence of the abductor muscles, with some opposing action of the adductors. In this position it is obvious that there can be no paralysis of either abductors or adductors, according to Semon's law.

Types of laryngeal paralysis.—Theoretically there might be a large variety of paralytic lesions of the larynx but, in point of fact, those encountered are relatively few. There seems no reason to doubt the truth of Semon's law, in spite of some criticisms of its accuracy. If it is accepted that the abductors are paralysed before the adductors, because they are more vulnerable, it follows that organic lesions of the adductors cannot occur as an isolated condition. Functional aphonia is merely a disordered action of the larynx, and not a form of paralysis, since the cords move well on arm efforts and during cough. Then again, there are described instances of paralysis affecting individual muscles—the thyro-arytenoid, the crico-arytenoideus lateralis and the interarytenoid—but these, if they occur, must be extremely rare, and in my experience none has appeared. There may, of course, be weakness of some of the sphincteric group, as in cases of tuberculosis, when the cords are bowed on phonation, but this is not an instance of paralysis, nor is the posterior gap sometimes left between the arytenoids paralytic, as it is merely the result of disordered phonation and can be corrected by re-education of the voice.

There remain to be considered, therefore, instances of paralysis of the recurrent laryngeal nerve, affecting either the abductors alone or all of the intrinsic group, and secondly cases where the crico-thyroid muscles are also involved. *Unilateral abductor paralysis* is frequently seen, and requires no particular comment, except to note the position of the aryepiglottic fold, and particularly the Wrisberg cartilage, which has sometimes been mistaken for a neoplasm, owing to its unusual bulbous appearance [6]. The affected vocal cord takes up a median position; during phonation the glottis is well closed, the healthy cord coming in to the mid-line, with the Wrisberg cartilage of the unaffected side passing in front of its paralysed neighbour (fig. 2, diagram 3). *Bilateral abductor paralysis* has already been referred to as leaving a glottic chink, but on inspiration there is naturally distressing dyspnœa, owing to the valvular nature of the glottic margins, which leads to their indrawing during inspiration (fig. 2, diagram 4). In *complete paralysis of the recurrent nerve* the paramedian position is taken up under the influence of the crico-thyroids. There is, therefore, a slight gap during phonation when the healthy cord comes to the mid-line, but, later, overaction of the unaffected cord may restore the voice almost to normal. *Complete bilateral recurrent paralysis,* leaving both cords in the paramedian position, allows air to pass with little distress through the narrowed glottis. The margins of the cords are still regular, although bowing outwards on expiration (fig. 2, diagrams 5 and 6).

Unilateral paralysis of the superior laryngeal nerve may follow operative injury or involvement in a new growth; it leads to lack of tension in the affected cord. *Bilateral paralysis* affecting these nerves is very rare.

When the *superior laryngeal nerve* is involved as well as the recurrent, *in combined paralysis,* the cadaveric position is taken up, as already described [3]; the margin of the affected vocal cord is irregular and wavy owing to flaccidity of the thyro-arytenoid muscles supporting it. There is naturally a sufficiently wide glottis for respiration, but during phonation there is feebleness of the voice owing to air waste, through the inability of the unaffected cord to close the glottis (fig. 2, diagram 7). Such a paralysis may follow a variety of causes, either in the basal nuclei, at the jugular foramen, or in the neck. I have seen instances due to many varying conditions, such as thrombosis of the posterior inferior cerebellar artery, fracture at the base of the skull with involvement of the jugular foramen, a tumour growing from the nasopharynx, and hæmorrhage in the neck following a bomb wound. Owing to the situation of the lesion, there is usually involvement of other nerves—the ninth, eleventh or twelfth—according to the location of the cause in the nuclei, at the base of the skull, or in the parapharyngeal space.

Bilateral combined paralysis is most unlikely to be seen, as a lesion involving the vagus on both sides is difficult to imagine.

The points of importance suggested for consideration are the necessity for clear expression regarding the paramedian and cadaveric positions, and the differentiation between recurrent laryngeal paralysis and what I would suggest should be called combined paralysis, when both branches of the vagus are involved.

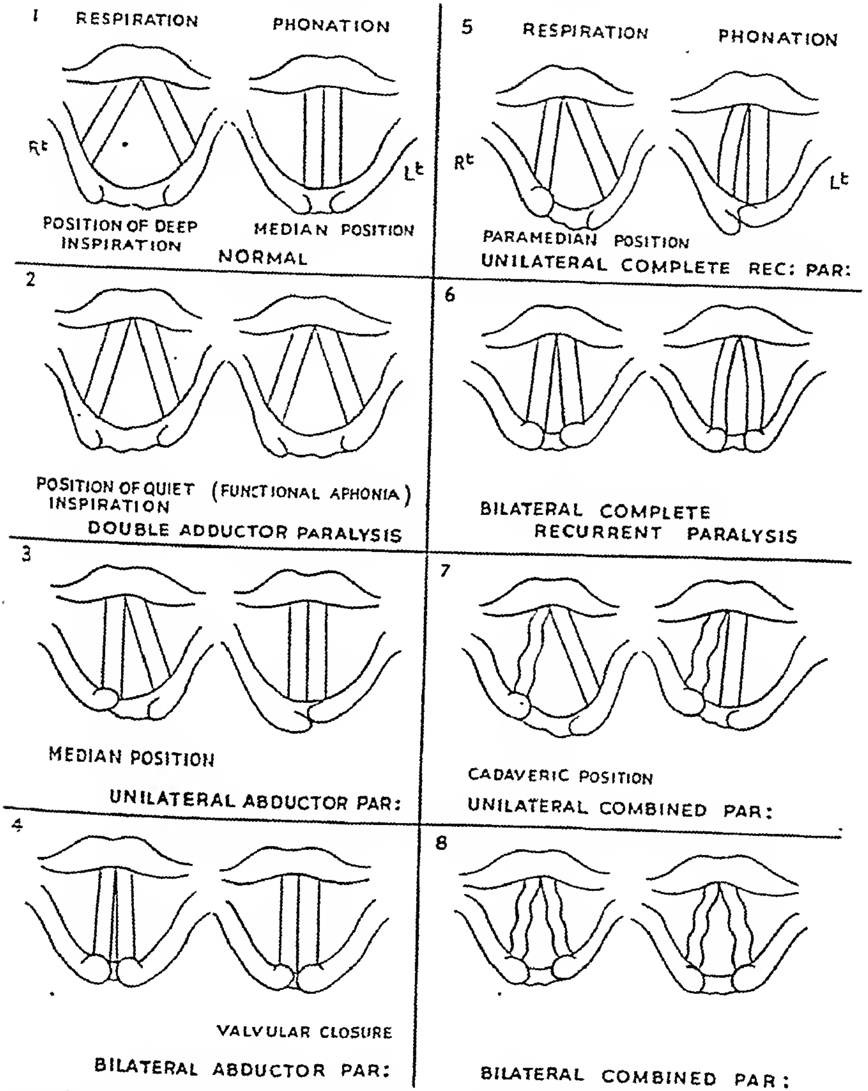

1 RESPIRATION
PHONATION
Rt
Lt
POSITION OF DEEP INSPIRATION
MEDIAN POSITION
NORMAL
2
POSITION OF QUIET INSPIRATION
(FUNCTIONAL APHONIA)
DOUBLE ADDUCTOR PARALYSIS
3
MEDIAN POSITION
UNILATERAL ABDUCTOR PAR:
4
VALVULAR CLOSURE
BILATERAL ABDUCTOR PAR:
5 RESPIRATION
PHONATION
Rt
Lt
PARAMEDIAN POSITION
UNILATERAL COMPLETE REC: PAR:
6
BILATERAL COMPLETE RECURRENT PARALYSIS
7
CADAVERIC POSITION
UNILATERAL COMBINED PAR:
8
BILATERAL COMBINED PAR:

FIG. 2.—Diagrams to illustrate the appearances of the larynx in paralytic conditions. In each, inspiration is represented on the left and phonation on the right. The overhanging position of the aryepiglottic fold and cartilage of Wrisberg is often more exaggerated than illustrated above.

(Figs. 1 and 2 appear in "Diseases of the Nose and Throat" by StClair Thomson and V. E. Negus, 5th Ed., and are reproduced by kind permission of the publishers, Messrs. Cassell & Co., Ltd., London.)

REFERENCES

1 WEDDELL, G. (1942) Personal Communication.
2 LEMERE, F. (1932) *Amer. J. Anat.*, 51, 417; (1933) *Arch. Otolaryng., Chicago*, 18, 413; (1934) *Ann. Otol. Rhin. Laryng.*, 43, 523.
3 CLERF, L. H., and SUEHS, O. W. (1941) *Ann. Otol. Rhin. Laryng.*, 50, 762.
4 LEDERER, F. L. (1943) Diseases of the Ear, Nose and Throat, Philadelphia, 4th Ed.
5 HOFER, G., and JESCHEK, J. (1940) *Z. f. Hals-Nas. u. Ohrenheilk.*, 45, 401.
6 COLLEDGE, L. (1935) Encycl. Brit. Med. Practice., Ed. Rolleston, H., London, 7, 612.

The Treatment of Subacute Maxillary Sinusitis Especially in Children

By G. E. ARCHER

SUBACUTE maxillary sinusitis may be defined as the prolongation of an acute infection of the maxillary sinus which has either not been treated or failed to yield to conservative treatment.

The idea that drainage from this cavity is by gravity and that the ostium is situated in a most unsuitable position for this purpose has largely influenced our thinking and surgical procedures have mostly been designed to provide gravitational drainage. Research has shown that gravity is probably not the most important factor in the removal of fluid from the sinus. Lowndes Yates, Proetz and others [1] have shown that the action of the ciliated mucous membrane within the sinus is probably the most important factor in removing secretion. Also that the ciliary action always works towards the natural ostium.

In 1933 O'Malley [2] demonstrated the importance of the ventilation of the maxillary sinus and showed that air pressures within the sinus rise and fall with inspiration and expiration. These pressure variations can be demonstrated not only in normal sinuses but in conditions of acute and chronic sinusitis. The rise and fall of pressure within the maxillary antrum synchronizes with the rise and fall of pressure within the nasal chambers, but would appear to be further emphasized by the middle turbinate overlying the maxillary ostium, thus a condition of affairs comparable to the Sprengel pump is produced so that during expiration the expired air passing forward through the nose will assist in evacuating the air from the maxillary sinus. Simon [3] published some investigations on this question and found that with the presence of a large ostium or accessory ostium the pressure readings in the antrum tended to equal those of the corresponding nasal fossa. From this it would appear that the making of a permanent ostium from the maxillary sinus into the inferior meatus of the nose will interfere with the normal variations of the pressures and with the ventilation of the sinus, and also (except when gross amounts of fluid are present in the sinus) the opening in the inferior meatus would appear unnecessary as the ciliary action will remove the fluid via the natural ostium.

It may be asked then is it necessary, or even desirable, to make a new permanent ostium from the inferior meatus into the antrum?

The generally accepted treatment for subacute sinusitis is repeated sinus lavage. In Jacksons' book [4] the condition is dismissed in one paragraph:

"Subacute maxillary sinusitis: This condition is a prolongation of an acute infection, and treatment is similar to that in the acute infection. If, after a few weeks, there is no improvement, it may be assumed that drainage from the sinuses is inadequate. These cases usually clear up following intranasal antrotomy in the inferior meatal wall".

In their book [5] StClair Thomson and Negus inform us that treatment by lavage is worth a trial; this three times a week for three weeks is suggested, but to discontinue if there is no decided improvement after six treatments, and that it is rarely curative in cases of more than six months' duration. My view is that most of us would now be inclined to persevere with antral lavage for considerably more than three weeks. One must admit that repeated antral puncture becomes irksome to the patient and he presses for a more rapid cure of his troubles.

Various other treatments (with or without antral lavage) have at different times been recommended. Proetz displacement therapy when first introduced was thought to be a great step forward, and it seemed as if this would solve the problem of curing the less tractable acute or subacute sinusitis. My own experience of this has resulted in only moderate success. Bauwens [6] made claims for the resolution of sinusitis by treatment with short-wave diathermy but it seems to me to be particularly difficult to assess the value of this treatment. My impression is that in some cases recovery may have been hastened but I feel that recovery might have resulted without short-wave treatment. The introduction of penicillin into the sinuses has been recommended. Angell James [7] suggested the use of penicillin paste. Hunt Williams [8] suggested the technique whereby an indiarubber ureteric catheter was introduced into the maxillary antrum through which perfusion of the sinus with penicillin could be carried out.

Some ten years ago I commenced the treatment of cases of maxillary sinus suppuration (especially in children) by the introduction of an indwelling rubber catheter (of the de Pezzer type) into the maxillary sinus from the inferior meatus of the nose. Through this the sinus was irrigated with normal saline two or three times a day for seven to ten days, and when repeated washings were returned clear the catheter was removed. I was greatly interested therefore when some time later I discovered an article in the *Archives of Otolaryngology* of 1926 by Alden [9] describing a similar procedure to the one I had adopted. He used short rubber tubes with a flange made for the purpose; irrigation was made with a bulb syringe, and the antrum was flushed with 1% mercurochrome or 2% silver nitrate solution. He recommended this daily irrigation until the sinus was free from secretion, usually a period of from ten to fourteen days. But I can find no evidence that this treatment was generally adopted. In 1937 Asherson [10] recommended in cases of acute maxillary sinusitis leaving a cannula in the antrum and projecting from the nose, through which repeated perfusion with saline was made.

The small operation I recommend is most satisfactorily performed under local anæsthesia except in the case of young children when a short general anæsthetic is advisable. After cocainizing the nose, a Killian's speculum is introduced under the inferior turbinate, which is gently elevated until a good view of the naso-antral wall is obtained. Thornwaldt's trephine is placed in the position in which an antral puncture is made where the bone is thinnest. After one or two turns the trephine slips into the antrum. The trephine is then withdrawn and a de Pezzer catheter of suitable size is introduced through the hole so made. It is rarely necessary to enlarge this opening. The catheter is fixed to the cheek with adhesive tape and its free end buried in a gauze pad to absorb any fluid seeping up from the antrum. The whole procedure is completed in one or two minutes. The following day irrigation with warm normal saline is commenced by attaching the Watson-Williams syringe to the catheter and allowing the fluid to flow out through the ostium. After several irrigations the washings are returned clear and then the catheter is withdrawn, after which the hole closes in a few days and the normal anatomy and physiology of the sinus are restored.

The only mishaps encountered have been in three cases where the end of the catheter broke in the antrum (probably due to old and perished indiarubber as new catheters were not easily obtained during the war years). In two of the cases no difficulty was experienced in removing the broken-off portion via the nose. In one case, a small child, it was necessary to open the antrum from the canine fossa.

The patients find this treatment in no way irksome and young children tolerate it perfectly well. Of course, in addition to this procedure, attention must be paid to other factors which may contribute to the chronicity of the condition. Any dental root infection must have attention, and in children, if there is a large adenoid mass interfering with efficient nasal respiration or harbouring infection, removal is indicated. In adults, if there is marked deflection of the septum towards the side of the diseased antrum, a submucous resection operation may be required. In these circumstances infraction of the middle turbinate would appear to be necessary in most cases.

Regarding diagnosis of the condition, the presence of pus demonstrated in the sinus washings would appear to be sufficient, always bearing in mind the possible pitfall that we may be dealing with a so-called pyosinus which is acting as a reservoir for pus draining from an infection of the upper sinuses.

By this method I have treated about 150 cases. The record submitted does not include Service patients treated in E.M.S. Hospitals as it is quite impossible to trace them all. The 100 cases analysed are those treated in private practice (39 cases), at the Manchester Northern Hospital (34 cases), and at Stockport Infirmary (27 cases) up to the early part of this year (1947). The more recent cases are not included as it is too soon to assess results. A questionnaire (viz. "Are you cured?" "Improved?" "Left the same?" "Made worse?") was sent to the first 100 patients. Ninety-five replied and all except three have been examined within the last month. Five have not been traced, or have not replied and therefore have not been examined.

TABLE I.—AGE AND SEX DISTRIBUTION

Age (years)	M.	F.	Total
Under 10.. ..	3	3	6
10–15	8	10	18
15–20	5	7	12
20–30	3	9	12
30–40	8	16	24
40–50	11	7	18
50 upwards ..	7	3	10
Total	45	55	100

TABLE II.—PREDOMINANT ORGANISMS

Bacteriological examination has not been made in every case unfortunately; a few records have been lost but pus was present in the antral washing in every case.

The organisms predominant were:

Staphylococci ..	14	Gram+cocci ..	3
Pneumococci ..	8	*H. influenzæ* ..	2
Streptococci ..	6	Gram-bacilli ..	2
B. catarrhalis ..	6	Diphtheroids ..	1

TABLE III.—RESULTS OF TREATMENT

These are based upon patients' replies and subsequent examination. The patients' impressions and the physical signs on examination correspond so closely that it is not necessary to separate them. The examination has included further X-ray examination and sinus washings in doubtful cases.

Results	Cured	Improved	Unchanged	No record
Private patients, 39				
Age: Under 10	2	—	—	—
10–15	5	—	1	—
15–20	3	1	—	—
20–30	4	—	—	—
30–40	5	3	—	—
40–50	8	2	—	—
50–	4	—	—	1
	31	6	1	1
Manchester Northern Hospital, 34				
Age: Under 10	—	1	—	—
10–15	4	2	2	—
15–20	2	2	1	—
20–30	1	1	—	1
30–40	5	2	—	2
40–50	4	2	—	—
50–	2	—	—	—
	18	10	3	3
Stockport Infirmary, 27				
Age: Under 10	1	2	—	—
10–15	2	2	—	—
15–20	1	1	1	—
20–30	3	1	1	—
30–40	3	3	—	1
40–50	1	1	—	—
50–	1	2	—	—
	12	12	2	1
Totals	61	28	6	5 = 100

TABLE IV.—RESULTS ANALYSED BETWEEN UNCOMPLICATED AND COMPLICATED CASES

Results	Cured	Improved	Unchanged	No record
Uncomplicated	24	12	—	2
Deflected septum no polypi ..	20	3	2	—
With nasal polypi	11	10	1	—
Asthma or bronchiectasis ..	2	2	2	1
With acute frontal sinusitis ..	—	1	—	—
Pansinusitis	—	—	1	—
Previous operation on nose and tonsillectomy	4	—	—	1
No record	—	—	—	1
Totals	61	28	6	5

TABLE V.—RESULTS ANALYSED ACCORDING TO DURATION OF DISEASE AND SYMPTOMS

I have found it extremely difficult to determine with any degree of accuracy the duration of the disease. The figures are based upon notes from patients' or doctors' statements.

Duration		Cured	Improved	Unchanged	No record
Under 1 month	Uncomplicated	3	—	—	—
	Complicated	—	1	—	—
1–6 months	Uncomplicated	6	—	—	—
	Complicated	2	3	1	—
6–12 months	Uncomplicated	5	2	—	—
	Complicated	5	1	2	—
Over 1 year	Uncomplicated	9	7	—	1
	Complicated	28*	11†	2	3
Unknown	Uncomplicated	1	3	—	1
	Complicated	2	—	1	—
Totals		61	28	6	5

*28 (18 deflected nasal septum: submucous resection; 10 nasal polypi removed).

†11 (2 deflected nasal septum: submucous resection; 7 nasal polypi removed; 2 asthma, bronchiectasis).

The numbers are far too small to make positive deductions but some of the results seem to be significant.

(i) In uncomplicated cases: Up to one year's duration, 14 cured, 2 improved; over one year's duration, 9 cured, 7 improved.

(ii) Cases of over one year's duration complicated by deflected septum: 18 cured; complicated with polypi, 10 cured.

Twenty-eight cases of maxillary sinus suppuration of over one year's duration, after submucous resection operation on the septum and infraction of the middle turbinal, or after removal of polypi from the middle meatus, in order to allow the sinus to drain by its ostium, were cured without any counter-drainage opening having been made. This seems to emphasize the importance of making certain that the normal ostium is patent and capable of allowing the secretion to pass out from the antrum into the middle meatus of the nose.

Have we underestimated the powers of recovery of the ciliated mucosa of the antrum, and would it not appear that the more frequent washing out of the purulent secretion so that the ciliary action may start again with as little delay as possible is one of the secrets of securing a good result? I feel that the findings justify further trial.

The period of treatment may be considerably shortened as most uncomplicated cases of maxillary suppuration will clear up in seven to ten days and the patient spared repeated antral puncture three or more times a week for a period of some weeks. This is particularly useful in children and adolescents where only one short anæsthetic is required. My experience is that even in quite young children antral puncture can be carried out without an anæsthetic, but if repeated the child, although not hurt, becomes apprehensive and suffers some degree of mental strain.

This treatment may dispense with the necessity of an intranasal antrostomy, particularly to be avoided in a child. A child's nose is very small and with the limited space available the operation is not easy. It is not uncommon to find adhesions between the turbinates and the septum after any operative procedure in a child's nose. My own view is that even if a permanent intranasal antrostomy has to be performed the inferior turbinate should be retained entire, but how often does one see the anterior portion sacrificed with subsequent hypertrophy of the posterior remaining part.

The disadvantages that may be urged against this treatment are: (i) That it is necessary to admit the patient to hospital. There may be reasons against this in the case of an adult, but surely it is far better to do so in the case of a child.

(ii) The condition of affairs within the antrum cannot be determined by vision. This does not seem so necessary in a child, but it must be admitted that it is desirable in any intractable case in an adult, especially if the condition is unilateral.

The ideal should surely be to cure the disease and restore the normal anatomy and physiology of the part. By this method no mucous membrane is sacrificed and the normal anatomy and physiology of the nose are maintained or restored.

REFERENCES

1 (*a*) Yates, A. Lowndes (1924) *Proc. R. Soc. Med.*, 17 (Sects. Laryng. and Otol., 8); (*b*) Proetz (1934) *J. Laryng.*, 49, 557.
2 O'Malley, J. P. (1933) *J. Laryng.*, 48, 309.
3 Simon, E. (1944) *Arch. Otolaryng., Chicago*, 39, 504.
4 Jackson, C., and Jackson, C. L. (1945) Diseases of the Ear, Nose and Throat. Philadelphia and London, p. 43.
5 Thomson, StClair, and Negus, V. E. (1937) Diseases of the Nose and Throat. London, p. 232.
6 Bauwens, P. (1938) *Proc. R. Soc. Med.*, 31, 891.
7 James, Angell (1941) *Proc. R. Soc. Med.*, 34, 671.
8 Williams, R. H. Hunt (1946) *Proc. R. Soc. Med.*, 39, 280.
9 Alden, A. M. (1926) *Arch. Otolaryng., Chicago*, 4, 521.
10 Asherson, N. (1937) *Lancet* (i), 1399.

The President said that he was all in favour of repeated puncture and the avoidance when possible of an operation. If the condition could be cured by such means it was a great advantage, and if by substituting Mr. Archer's method less distress was occasioned to the patient that also was all to the good. The line of treatment recommended was to his mind quite reasonable.

Mr. James Crooks said that during the twelve months to the end of May last 570 children under 12 years of age—new patients—were referred to his department at Great Ormond Street with X-ray films showing opacity of the antrum. They were all washed out under local anæsthesia, and of the 570, as many as 230 were clear at their first washing. The other 340 had mucopus in the antra, and went on to repeated washing. They continued this lavage ten or twelve times before they dreamed of doing anything else apart from local treatment. In going over the figures the other day his registrar told him that out of the 340 children only 9 were referred for operative treatment—that is to say, anything more radical than lavage. That did not mean that the 331 were all cured, but certainly the vast majority of them were cured on antral washing. It would be quite safe to

say that 250 of those 330 children with antral infection were cured by washing alone. That being so, he would be very loth indeed to adopt anything more radical, even making an opening large enough to take a de Pezza catheter, as had been suggested. It would be always advantageous not to take away the bone or mucosa, and he would think that washing was the right treatment for these children.

When he was forced to do more than lavage he had done the Caldwell-Luc operation, and he had been most depressed to find that in these young children—all under 12, many of them only 6 or 7 years of age—the changes in the mucosa were in no way inferior to the changes found in the adult with chronic suppuration. One was left with the impression on looking at the mucosa that nothing short of removal would have effected improvement. The children were a great deal better after the Caldwell-Luc operation, and that was an important point, because more than half these children had bronchiectasis or other chronic lung conditions. Of the 61 children who underwent the Caldwell-Luc operation, on 53 of whom the bilateral operation was performed, bronchiectasis was present in 34.

He mentioned that he had on occasion inserted a ureteric catheter through the ordinary cannula after puncture of the antrum, keeping it there for ten days, and running in penicillin to the antrum. He had not found it beneficial, nor had he found it helpful to give massive doses of systemic penicillin. The right thing to do for a child with subacute sinus infection was to send him to a seaside resort for a month with shrinking drops for the nose, and then, if the antrum still gave trouble, to wash it out. He would wash out the antrum twelve times before he did anything else—and then he thought he would wait six months and wash it out again. After that he might be persuaded into doing the Caldwell-Luc operation. Lavage alone would cure the vast majority of these children who had had sinusitis for a month or two.

Mr. Scott Stevenson deprecated the notion of washing out the nose with saline, which within his knowledge often caused otitis media. He had tried many years ago to cure cases of so-called nasal catarrh by washing out the nose and antra with antiseptics or saline, and putting in silver nitrate and similar preparations. But for years past he had done the Caldwell-Luc operation for chronic maxillary sinusitis, with no after-treatment at all, and this often, though not always, cleared up infection of the frontal and other sinuses by removing the chief focus of disease.

His chief criticism of the paper related to Mr. Archer's term the "subacute" case, but as he mentioned pus and polypi he himself would call such cases chronic. He had never yet found a case of maxillary sinusitis in a child in whom adenoids were not present, even when they were supposed to have been removed. He certainly would not like to wash out a child's antrum under local anæsthetics ten or twelve times, as Mr. Crooks did. What he had always carried out was thorough lavage of the antrum once at the time of operation with removal of adenoids, and he firmly believed that the removal of adenoids was what cleared up the sinusitis whether one did lavage or not.

Mr. G. E. Archer, in reply, said that Mr. Crooks had had a very wide experience and one must take notice of what he had said but it was particularly to avoid the repeated antral washings that Mr. Crooks advocated that he (Mr. Archer) had suggested putting in the self-retaining catheter. Some children would tolerate repeated antral puncture perfectly well but they had all seen the child who is extremely nervous and apprehensive and who resents repeated washings. He did not think the procedure he had recommended destroyed any more mucous membrane or any more bone than doing the antral puncture and one could wash out three or four times a day for three or more days and the case would clear up.

In replying to Mr. Scott Stevenson he said he had purposely called the cases subacute because the fact remained that some of these cases, although they had continued for a year or even more, had eventually been cured without a Caldwell-Luc operation being performed, and this was why he had felt justified in calling them subacute.

Film: "Bronchial Neoplasms", by PAUL H. HOLINGER, Chicago (shown by G. H. BATEMAN).

The film first shows endoscopic views of the normal larynx and tracheobronchial tree. It then shows various neoplastic disorders of the trachea and bronchi and correlates them with radiographs of the chest and associated disorders of the larynx. It finishes with an endoscopic view of a carcinoma of the mid-œsophagus and shows the bronchoscopic view of this same neoplasm invading the left main bronchus. The photography and colour are excellent and the film provides a perfect example of the bronchoscopist's view of typical bronchial neoplasms.

[*The Otological Session of the Summer Meeting will appear in the January issue of the "Proceedings".*]

Section of Neurology

President—DOUGLAS MCALPINE, M.D., F.R.C.P.

[*May* 1, 1947]

The Normal Temporal Horn and Its Deformities by Tumours in the Middle Cerebral Fossa. [*Abstract*][1]

By ERIK LINDGREN, M.D.

(*From the Roentgen Department, Serafimer Hospital, Stockholm*)

IN the medial portion of the temporal lobe lies the inferior, or temporal, horn. It roughly follows the curve of the hippocampus and ends about 2·5 cm. from the tip of the lobe. The anterior part of the horn is directed medially. The floor of the horn is mainly formed by the hippocampus and laterally by the collateral eminence. A small part of the roof is formed by the tail of the caudate nucleus. In its neighbourhood is the optic radiation.

Childe and Penfield divide the horn in two parts, one above the hippocampus, which they call the supracornual cleft, and one lateral, which they call the body, but which I prefer to call the lateral cleft. In the supracornual cleft lies the choroid plexus. The lateral and supracornual cleft join each other at the tip of the horn. Very occasionally, a more or less thin membrane passes between the supracornual and the lateral cleft to the lateral part of the hippocampus. In the three cases observed by the author, this septum appeared only in the anterior part of the horn.

For pneumographic examinations of the temporal horn there are two methods for filling the horn with gas. In a lateral X-ray picture, taken with the patient lying down and with the head turned to the side, the upper temporal horn is usually easily recognized, if sufficient gas is present. In 1934, Torkildsen and Pirie modified this technique. They first placed the patient in the position described and then they lowered the top of the head a little and turned the face upwards at an angle of 30 degrees. In our opinion, the essential demands on positioning in radiology are, first, that the position must be an easy one to assume, secondly that it is easy to reproduce and thirdly that it gives a true picture of the anatomy. The positions just mentioned are not satisfactory in these respects, as it is impossible to be quite sure that there is sufficient gas in the horn, even if there is a large amount of gas in the ventricles, and because the anatomical details will be only partly visible. We have therefore adopted another method for filling the horn (demonstrated by cinematography at the lecture) and we use a different radiographic technique. Pictures taken with the different methods are not directly comparable, as is seen in fig. 1 (overleaf). With the head in sideway position, the air is in the lateral uppermost part of the horn and the cerebrospinal fluid in the lowermost part, i.e. the gas occupies chiefly the lateral cleft. With the patient in supine position, the horn gets completely filled with gas, if sufficient is present. On the side view, taken with the patient in supine position, the supracornual cleft is seen as a darker strip on the film, as the rays have gone through a deeper layer of gas. Below the supracornual cleft is a thinner layer of gas, representing the lateral cleft. The point where the supracornual cleft starts to bend down over pes hippocampus to join the lateral cleft I call the "knee". I have given it a special name, because in certain pathological conditions this knee is more or less accentuated and it might be the only demonstrable radiological change. The inclination of the horn is dependent on the shape of the skull. With a short skull the inclination is sharper than in a long skull. When we regard the horn obliquely from above (on a picture taken with 25–35 degrees inclination) it has the shape of a spoon, the shaft of which is formed by the lateral cleft.

On an anteroposterior picture the lateral cleft is always the easiest to observe and very sharply defined. If the picture is taken with the chin higher up than usual, we get a more axial view of the horn. In this projection, the picture is more like an ordinary frontal section through the brain. This projection is the best one for a close study of the anatomical details.

---

[1] The complete report of this investigation will appear as a supplement to *Acta Radiologica*, 1948.

say that 250 of those 330 children with antral infection were cured by washing alone. That being so, he would be very loth indeed to adopt anything more radical, even making an opening large enough to take a de Pezza catheter, as had been suggested. It would be always advantageous not to take away the bone or mucosa, and he would think that washing was the right treatment for these children.

When he was forced to do more than lavage he had done the Caldwell-Luc operation, and he had been most depressed to find that in these young children—all under 12, many of them only 6 or 7 years of age—the changes in the mucosa were in no way inferior to the changes found in the adult with chronic suppuration. One was left with the impression on looking at the mucosa that nothing short of removal would have effected improvement. The children were a great deal better after the Caldwell-Luc operation, and that was an important point, because more than half these children had bronchiectasis or other chronic lung conditions. Of the 61 children who underwent the Caldwell-Luc operation, on 53 of whom the bilateral operation was performed, bronchiectasis was present in 34.

He mentioned that he had on occasion inserted a ureteric catheter through the ordinary cannula after puncture of the antrum, keeping it there for ten days, and running in penicillin to the antrum. He had not found it beneficial, nor had he found it helpful to give massive doses of systemic penicillin. The right thing to do for a child with subacute sinus infection was to send him to a seaside resort for a month with shrinking drops for the nose, and then, if the antrum still gave trouble, to wash it out. He would wash out the antrum twelve times before he did anything else—and then he thought he would wait six months and wash it out again. After that he might be persuaded into doing the Caldwell-Luc operation. Lavage alone would cure the vast majority of these children who had had sinusitis for a month or two.

Mr. Scott Stevenson deprecated the notion of washing out the nose with saline, which within his knowledge often caused otitis media. He had tried many years ago to cure cases of so-called nasal catarrh by washing out the nose and antra with antiseptics or saline, and putting in silver nitrate and similar preparations. But for years past he had done the Caldwell-Luc operation for chronic maxillary sinusitis, with no after-treatment at all, and this often, though not always, cleared up infection of the frontal and other sinuses by removing the chief focus of disease.

His chief criticism of the paper related to Mr. Archer's term the "subacute" case, but as he mentioned pus and polypi he himself would call such cases chronic. He had never yet found a case of maxillary sinusitis in a child in whom adenoids were not present, even when they were supposed to have been removed. He certainly would not like to wash out a child's antrum under local anæsthetics ten or twelve times, as Mr. Crooks did. What he had always carried out was thorough lavage of the antrum once at the time of operation with removal of adenoids, and he firmly believed that the removal of adenoids was what cleared up the sinusitis whether one did lavage or not.

Mr. G. E. Archer, in reply, said that Mr. Crooks had had a very wide experience and one must take notice of what he had said but it was particularly to avoid the repeated antral washings that Mr. Crooks advocated that he (Mr. Archer) had suggested putting in the self-retaining catheter. Some children would tolerate repeated antral puncture perfectly well but they had all seen the child who is extremely nervous and apprehensive and who resents repeated washings. He did not think the procedure he had recommended destroyed any more mucous membrane or any more bone than doing the antral puncture and one could wash out three or four times a day for three or more days and the case would clear up.

In replying to Mr. Scott Stevenson he said he had purposely called the cases subacute because the fact remained that some of these cases, although they had continued for a year or even more, had eventually been cured without a Caldwell-Luc operation being performed, and this was why he had felt justified in calling them subacute.

Film: "Bronchial Neoplasms", by PAUL H. HOLINGER, Chicago (shown by G. H. BATEMAN).

The film first shows endoscopic views of the normal larynx and tracheobronchial tree. It then shows various neoplastic disorders of the trachea and bronchi and correlates them with radiographs of the chest and associated disorders of the larynx. It finishes with an endoscopic view of a carcinoma of the mid-œsophagus and shows the bronchoscopic view of this same neoplasm invading the left main bronchus. The photography and colour are excellent and the film provides a perfect example of the bronchoscopist's view of typical bronchial neoplasms.

[*The Otological Session of the Summer Meeting will appear in the January issue of the "Proceedings".*]

Section of Neurology

President—DOUGLAS MCALPINE, M.D., F.R.C.P.

[*May* 1, 1947]

The Normal Temporal Horn and Its Deformities by Tumours in the Middle Cerebral Fossa. [*Abstract*][1]

By ERIK LINDGREN, M.D.
(*From the Roentgen Department, Serafimer Hospital, Stockholm*)

IN the medial portion of the temporal lobe lies the inferior, or temporal, horn. It roughly follows the curve of the hippocampus and ends about 2·5 cm. from the tip of the lobe. The anterior part of the horn is directed medially. The floor of the horn is mainly formed by the hippocampus and laterally by the collateral eminence. A small part of the roof is formed by the tail of the caudate nucleus. In its neighbourhood is the optic radiation.

Childe and Penfield divide the horn in two parts, one above the hippocampus, which they call the supracornual cleft, and one lateral, which they call the body, but which I prefer to call the lateral cleft. In the supracornual cleft lies the choroid plexus. The lateral and supracornual cleft join each other at the tip of the horn. Very occasionally, a more or less thin membrane passes between the supracornual and the lateral cleft to the lateral part of the hippocampus. In the three cases observed by the author, this septum appeared only in the anterior part of the horn.

For pneumographic examinations of the temporal horn there are two methods for filling the horn with gas. In a lateral X-ray picture, taken with the patient lying down and with the head turned to the side, the upper temporal horn is usually easily recognized, if sufficient gas is present. In 1934, Torkildsen and Pirie modified this technique. They first placed the patient in the position described and then they lowered the top of the head a little and turned the face upwards at an angle of 30 degrees. In our opinion, the essential demands on positioning in radiology are, first, that the position must be an easy one to assume, secondly that it is easy to reproduce and thirdly that it gives a true picture of the anatomy. The positions just mentioned are not satisfactory in these respects, as it is impossible to be quite sure that there is sufficient gas in the horn, even if there is a large amount of gas in the ventricles, and because the anatomical details will be only partly visible. We have therefore adopted another method for filling the horn (demonstrated by cinematography at the lecture) and we use a different radiographic technique. Pictures taken with the different methods are not directly comparable, as is seen in fig. 1 (overleaf). With the head in sideway position, the air is in the lateral uppermost part of the horn and the cerebrospinal fluid in the lowermost part, i.e. the gas occupies chiefly the lateral cleft. With the patient in supine position, the horn gets completely filled with gas, if sufficient is present. On the side view, taken with the patient in supine position, the supracornual cleft is seen as a darker strip on the film, as the rays have gone through a deeper layer of gas. Below the supracornual cleft is a thinner layer of gas, representing the lateral cleft. The point where the supracornual cleft starts to bend down over pes hippocampus to join the lateral cleft I call the "knee". I have given it a special name, because in certain pathological conditions this knee is more or less accentuated and it might be the only demonstrable radiological change. The inclination of the horn is dependent on the shape of the skull. With a short skull the inclination is sharper than in a long skull. When we regard the horn obliquely from above (on a picture taken with 25–35 degrees inclination) it has the shape of a spoon, the shaft of which is formed by the lateral cleft.

On an anteroposterior picture the lateral cleft is always the easiest to observe and very sharply defined. If the picture is taken with the chin higher up than usual, we get a more axial view of the horn. In this projection, the picture is more like an ordinary frontal section through the brain. This projection is the best one for a close study of the anatomical details.

---

[1] The complete report of this investigation will appear as a supplement to *Acta Radialogica*, 1948.

say that 250 of those 330 children with antral infection were cured by washing alone. That being so, he would be very loth indeed to adopt anything more radical, even making an opening large enough to take a de Pezza catheter, as had been suggested. It would be always advantageous not to take away the bone or mucosa, and he would think that washing was the right treatment for these children.

When he was forced to do more than lavage he had done the Caldwell-Luc operation, and he had been most depressed to find that in these young children—all under 12, many of them only 6 or 7 years of age—the changes in the mucosa were in no way inferior to the changes found in the adult with chronic suppuration. One was left with the impression on looking at the mucosa that nothing short of removal would have effected improvement. The children were a great deal better after the Caldwell-Luc operation, and that was an important point, because more than half these children had bronchiectasis or other chronic lung conditions. Of the 61 children who underwent the Caldwell-Luc operation, on 53 of whom the bilateral operation was performed, bronchiectasis was present in 34.

He mentioned that he had on occasion inserted a ureteric catheter through the ordinary cannula after puncture of the antrum, keeping it there for ten days, and running in penicillin to the antrum. He had not found it beneficial, nor had he found it helpful to give massive doses of systemic penicillin. The right thing to do for a child with subacute sinus infection was to send him to a seaside resort for a month with shrinking drops for the nose, and then, if the antrum still gave trouble, to wash it out. He would wash out the antrum twelve times before he did anything else—and then he thought he would wait six months and wash it out again. After that he might be persuaded into doing the Caldwell-Luc operation. Lavage alone would cure the vast majority of these children who had had sinusitis for a month or two.

Mr. Scott Stevenson deprecated the notion of washing out the nose with saline, which within his knowledge often caused otitis media. He had tried many years ago to cure cases of so-called nasal catarrh by washing out the nose and antra with antiseptics or saline, and putting in silver nitrate and similar preparations. But for years past he had done the Caldwell-Luc operation for chronic maxillary sinusitis, with no after-treatment at all, and this often, though not always, cleared up infection of the frontal and other sinuses by removing the chief focus of disease.

His chief criticism of the paper related to Mr. Archer's term the "subacute" case, but as he mentioned pus and polypi he himself would call such cases chronic. He had never yet found a case of maxillary sinusitis in a child in whom adenoids were not present, even when they were supposed to have been removed. He certainly would not like to wash out a child's antrum under local anæsthetics ten or twelve times, as Mr. Crooks did. What he had always carried out was thorough lavage of the antrum once at the time of operation with removal of adenoids, and he firmly believed that the removal of adenoids was what cleared up the sinusitis whether one did lavage or not.

Mr. G. E. Archer, in reply, said that Mr. Crooks had had a very wide experience and one must take notice of what he had said but it was particularly to avoid the repeated antral washings that Mr. Crooks advocated that he (Mr. Archer) had suggested putting in the self-retaining catheter. Some children would tolerate repeated antral puncture perfectly well but they had all seen the child who is extremely nervous and apprehensive and who resents repeated washings. He did not think the procedure he had recommended destroyed any more mucous membrane or any more bone than doing the antral puncture and one could wash out three or four times a day for three or more days and the case would clear up.

In replying to Mr. Scott Stevenson he said he had purposely called the cases subacute because the fact remained that some of these cases, although they had continued for a year or even more, had eventually been cured without a Caldwell-Luc operation being performed, and this was why he had felt justified in calling them subacute.

Film: "Bronchial Neoplasms", by PAUL H. HOLINGER, Chicago (shown by G. H. BATEMAN).

The film first shows endoscopic views of the normal larynx and tracheobronchial tree. It then shows various neoplastic disorders of the trachea and bronchi and correlates them with radiographs of the chest and associated disorders of the larynx. It finishes with an endoscopic view of a carcinoma of the mid-œsophagus and shows the bronchoscopic view of this same neoplasm invading the left main bronchus. The photography and colour are excellent and the film provides a perfect example of the bronchoscopist's view of typical bronchial neoplasms.

[The Otological Session of the Summer Meeting will appear in the January issue of the "Proceedings".]

the sphenoidal ridge and from the brain itself—the temporal lobe. The material forming the basis for this study consists of 104 cases. Of these 9 are basilar tumours, 6 meningiomas and 3 neurinomas. In the last 3 cases there was no dislocation of the septum pellucidum, or any general deformity of the ventricular system.

The temporal horn in all these cases was dislocated upwards. In the neurinomas there was a concavity directed downwards and medially (fig. 6) while in the meningiomas the horn was directed more straight downwards. If a glioma is situated in the temporal lobe, entirely below the horn, it is possible to differentiate from an extracerebral tumour only if the glioma has caused considerable irregularities of the floor of the horn.

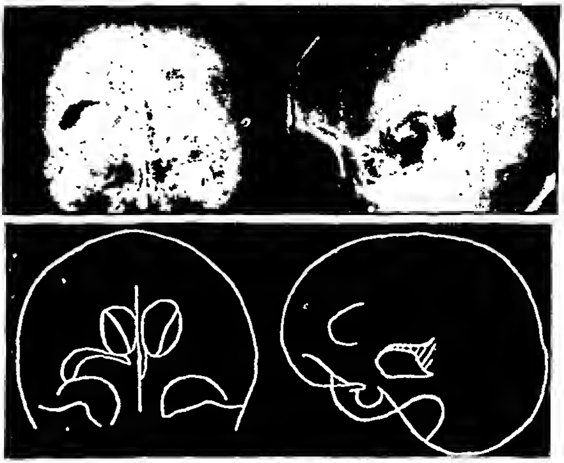


FIG. 6.—Neurinoma from the gasserian ganglion.

Tumours from the sphenoidal ridge are usually divided into three types: the clinoidal or deep type, tumours from the middle part and those from the lateral part and pterion. From the radiological standpoint, the pterion type is not uniform, as it is possible to distinguish between different types of deformities depending on how much of the tumour is situated in the middle cerebral fossa and how much above the sphenoidal ridge. The largest group consists of the type where most of the tumour lies in the middle cerebral fossa—in this material 22 out of 30 cases. It is characterized by a displacement medially of the anterior part of the temporal horn with compression of the lateral cleft (fig. 7). The other type (8 cases) has only a straightening out of the knee (fig. 8). The tumours which grow "en plaque" produce hyperostosis. The only deformity is a compression of the temporal horn from the front. The knee is more clearly distinguished than normally. Out of 4 cases, 1 had no general dislocation of the ventricular system and no visible change of the temporal horn on an antero-posterior picture.

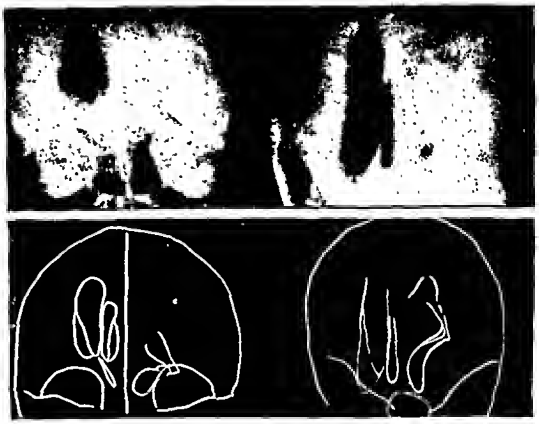


FIG. 7.—Meningioma from pterion (lower type).

Tumours from the middle part of the ridge compress the bowl of the spoon from the front, displace it backwards and give it a concave anterior border directed straight forward. The deformity is best seen on the half-axial view.

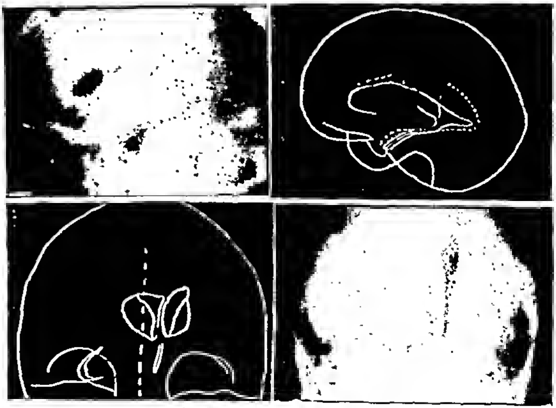


FIG. 8.—Meningioma from pterion (higher type).

The deep type are tumours from the medial part of the lesser sphenoidal wing and the anterior clinoid process. Out of 6 such cases, 1 has been localized entirely to the middle cerebral fossa. In this case the temporal horn has been pushed backwards and on the

The radiological diagnosis of a tumour in the middle cerebral fossa usually seems to be based on a general dislocation and deformity of the ventricular system and not on a thorough analysis of the shape of the temporal horn, with the result that in many cases we can only suspect the presence of a tumour. The exact pre-operative localization of a tumour which is so essential is not possible without a thorough examination of the temporal horn. Again, there may be large tumours in the middle cerebral fossa with no general dislocation of the ventricular system at all, only with a deformity of the temporal horn. Most tumours above the tentorium can produce a deformity of the temporal horn and a study of the shape of the horn makes a differentiation of the main deformities possible. The half-schematic drawings in figs. 2-5 illustrate this. Generally, the tumour is localized on the basis of the more obvious changes of the ventricular system. In some cases, the shape of the temporal horn gives valuable supplementary information, but for an exact localization of a tumour in the middle cerebral fossa, the shape of the temporal horn is of decisive importance.

Tumours in the middle cerebral fossa may be divided into tumours from the floor, from

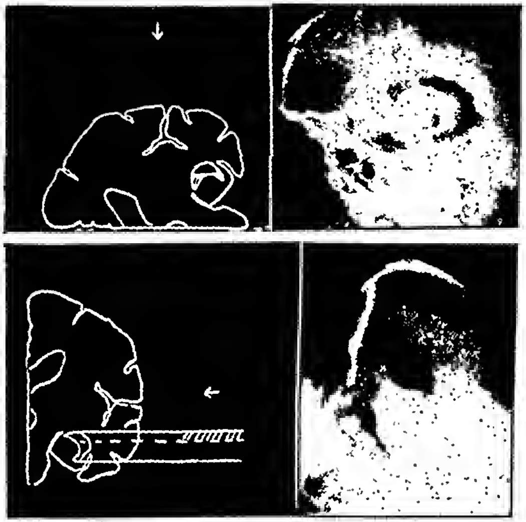


FIG. 1.—The striated portion of the upper schematic drawing represents the cerebrospinal fluid.

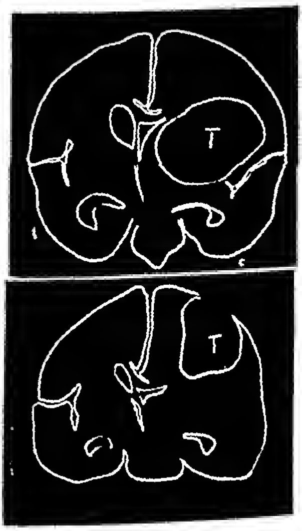


FIG. 2.

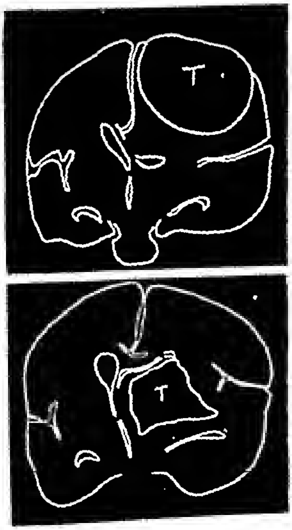


FIG. 3.

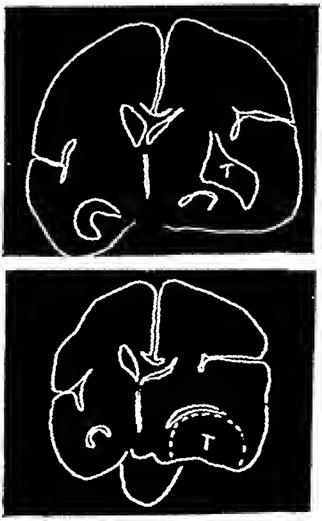


FIG. 4.

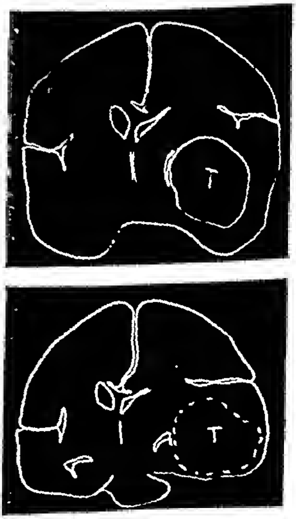


FIG. 5.

Section of Psychiatry

President—Professor Aubrey Lewis, M.D.

[*June* 10, 1947]

The Importance of Statistics in Psychiatry

By L. S. Penrose, M.D.

Galton Professor of Eugenics, University College, London

Abstract.—The paper gives an outline, with examples, of various statistical methods which may be of special use in psychiatry.

(1) *Actuarial data.*—The simple accumulation of accurate figures on the ages of patients, their diagnoses and length of stay in hospital or under treatment for mental illness is of great value in understanding the scope of psychiatric problems. The age and sex incidences which correspond to different disease groups are very characteristic. Such material has value in the estimation of the results of therapeutic experiments but special methods have to be devised, as there is no exact prototype in standard vital statistics or in work on therapeutic trials.

(2) *Biametric techniques.*—Knowledge of ordinary statistical practice guards against elementary errors and aids in establishing significance or otherwise of metrical deviations from the normal found in mentally ill subjects. Also the range of variations may be much more marked in abnormal than in normal groups. Furthermore, abnormal reactions in themselves may be characterized by either too much or too little variety, i.e. by scatter or by stereotypy.

Discrimination between normal and abnormal reaction can be based on a single quantitative measurement, on difference in variance or on a compound measurement, i.e. pattern or profile. The discriminative approach has advantages over other methods because in this approach the initial factors are concrete and based on known classes such as males and females, children and adults, special clinical types, &c.

(3) *Genetical analysis.*—Actuarial data can be useful in genetic studies by leading to estimation of population frequency of genes and consanguinity rates. Moreover, combined clinical and genetical observations can reveal the existence of new clinical entities.

Résumé.—Cet article expose dans ses grandes lignes les diverses méthodes statistiques qui peuvent être utiles en psychiatrie, avec quelques exemples.

(1) *Données actuarielles.*—La simple accumulation de données numériques exactes sur l'âge des malades, les diagnostics et la durée de leur séjour à l'hôpital ou de leur traitement pour une maladie mentale a une grande valeur en faisant comprendre la portée des problèmes psychiatriques. Les incidences selon l'âge et le sexe des différents groupes de maladies sont très caractéristiques. Un tel matériel est utile pour l'évaluation des résultats des essais thérapeutiques, mais il faut trouver de nouvelles méthodes, car il n'existe pas de prototype exact dans les statistiques vitales générales, ni de travail sur les essais thérapeutiques.

(2) *Techniques biamétriques.*—Une connaissance de la pratique statistique ordinaire permet d'éviter les erreurs élémentaires, et aide à reconnaître si une déviation de la normale chez un malade mental est significative ou non. Il est aussi possible que l'étendue des variations soit beaucoup plus grande dans les groupes anormaux que dans les groupes normaux. De plus, les réactions anormales elles-mêmes peuvent être caractérisées par trop ou trop peu de variété, c'est à dire par la dispersion ou par la stéréotypie.

La distinction entre les réactions normales et anormales peut être basée sur une seule mesure quantitative, sur une différence de variation ou sur une mesure composée, c'est à dire un groupement ou un profil.

La méthode différentielle a l'avantage sur les autres méthodes que les facteurs initiaux sont concrets et basés sur une classe connue, telle que hommes ou femmes, enfants ou adultes, types cliniques spéciaux, etc.

(3) *Analyse génétique.*—Les données actuarielles peuvent être utiles dans les études génétiques, en menant à l'estimation de la fréquence des gènes et de la consanguinité dans une population. En outre, la combinaison des observations cliniques et génétiques peut démontrer l'existence de nouvelles entités cliniques.

АБСТРАКТ.—Лекция дает отчет и примеры различных статистических методов специально применимых в психиатрии

1. Статистические данные.—Простое накопление точных чисел возрастов больных, их диагнозов и длительности пребывания в госпитале или же лечения душевной болезни, имеет большое значение в понимании целей психиатрических проблем. Отношение возраста и пола к разным группам болезней очень характерно. Такой материал очень важен для оценки результатов терапевтических опытов, но нужно найти специальные методы, так как нет точного прототипа в стандарте жизненных статистик или в работе над терапевтическими опытами.

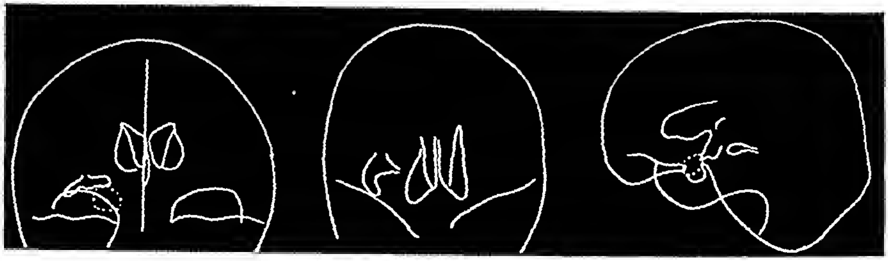


FIG. 9.—Meningioma of the clinoidal type, only in the middle cerebral fossa (dotted: bone sclerosis).

half-axial view there is a filling defect in the medial part of the spoon (fig. 9). In the other cases, the tumours extended into the anterior fossa, thereby causing the same deformity of the anterior horn as by subfrontal tumours and, besides, a straightening out of the knee of the temporal horn.

The tumours in the temporal lobe, gliomas, cause the most varying deformities of the horn, depending on their position in the lobe. In this material, we have 3 cases with no dislocation of the septum. No changes would have been established to allow a tumour diagnosis had the temporal horn not been examined. If a glioma is situated in the same place as is described for meningiomas, the pictures may be alike. In some cases it is therefore impossible to distinguish a meningioma from a glioma radiologically and we must content ourselves with localizing the tumour only. Generally speaking, all deformities which do not agree with those described, may be assumed to be caused by gliomas. In this material there are 42 gliomas. We could make the diagnosis of glioma in 23 cases. In 2 cases it was impossible to fill the horn and in 17 cases we could not state what kind of tumour had caused the changes.

Four cases of cholesteatomas have quite a characteristic appearance. The gas is lying distributed in larger or smaller irregular spots (fig. 10).

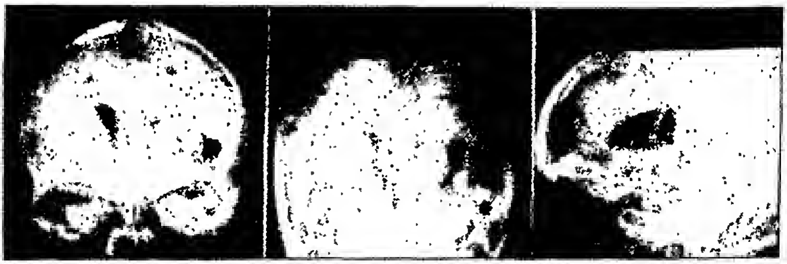


FIG. 10.—Cholesteatoma in the temporal horn.

During the last 14 years, we have had 4 cases where we could find no sign of a tumour in the temporal lobe by pneumographic examination, but where a tumour was revealed by arteriography or by calcification visible on the plain films. On the other hand, we have 2 cases where pneumography gave us the diagnosis but where the angiography failed. It is not yet possible to decide which method is the more reliable, but it seems to me that the answer is that one method may be used as a complement to the other.

Even the most thorough analysis of the anatomical details may sometimes fail. The more spreading a lesion is, the easier it is to observe; the more infiltrative, the harder to recognize. When tumours have reached such a size that they produce clinical symptoms, they are as a rule big enough to be discovered at a closer radiological examination. To get the best results, however, a pneumographic examination must be performed by an experienced radiologist.

We radiologists have, as it were, the opportunity of cutting sections *in vivo*. We must, however, extract the right sections. Just as pathologists will fail to arrive at the truth at autopsy, if they cut too few sections—or the incorrect sections—so will the radiologist fail by taking short cuts in his examination or, worse still, by relying only on the standard projections of a technician. When making use of X-rays, the radiologist has to choose appropriate projections for presenting the various anatomical details in each case, and this must be dependent upon the kind of deformities and the shape of the skull. If a lesion has not been brought out at the examination, an interpretation of the picture later will not succeed in exposing it, however thorough the study may be.

available, and came to the conclusion that the amount of attention paid to mental health was inversely proportional to the amount of serious crime (Penrose, 1939). Very roughly, two beds in a mental hospital made one prison cell unnecessary. As prisons cost twice as much as mental hospitals per inmate, there is approximate economical equivalence but social advantage is presumably with the hospital beds.

In the case of mental deficiency much could be learned if we knew the age grouping and intelligence distribution of all institutional cases. Table I shows a rough estimate of the distribution based on surveys of general and institutional populations. One can say that probably one-third of all idiots in the country are under institutional care, one-sixth of all imbeciles but only one-twentieth of all feeble-minded; and of the borderline cases only an extremely small fraction. It is evident that some very strong selective mechanisms determine just which cases shall be cared for and which left in the community. Undoubtedly, those whose families are in poor circumstances contribute an undue proportion of cases and, furthermore, patients with behaviour disorder added to defect are concentrated in the institutional group.

TABLE I.—DEFECTIVES OF ALL TYPES: ESTIMATED NUMBERS IN ENGLAND AND WALES

Grade	Total in general population	Institutional cases	Proportion in institutions
Borderline ..	?	5,000	1/....
Feeble-minded	300,000	15,000	1/20
Imbecile ..	80,000	13,000	1/6
Idiot	20,000	7,000	1/3
Total	400,000	40,000	1/10

Turning to the mentally ill, an elementary example of the value of actuarial data is the difference found in proportions of diagnoses according to whether we consider first admissions or resident populations. The trends are shown in Table II (Duncan *et al.*, 1936). The longer a patient stays in hospital the more likely is he to be a diagnosed schizophrenic, even if he did not start with this diagnosis. In general, diagnosis in psychiatry is so elusive that the age and sex of patients on first admission, which is a very good guide, cannot be neglected. The cases fall naturally into four classes, which have their maximum frequencies in the four double decades 0 to 20, 20 to 40, 40 to 60, 60 to 80. The classes are, mental defect, schizophrenia, affective psychosis and organic psychosis. Fig. 1 (p. 866) shows the relationship of diagnosis and age in 9,821 patients first admitted to the Ontario mental hospitals during the years 1939 to 1942. For simplicity here, epilepsy has been grouped with mental defect and some miscellaneous diagnoses have been included with the organic. Specifying sex gives further information. There are relatively more male cases of early onset and of late onset than female cases, who, in their turn, are more frequent in the central period, 30 years to 50 years. Classification according to both diagnosis and sex helps to explain this phenomenon. Schizophrenia (like mental defect) is more severe in males than in females as shown by its earlier onset in the male sex. Malzberg's (1935) survey of admissions to New York State Mental Hospitals is typical of all large bodies of data in this respect. He found that the mean first admission age for male cases of dementia præcox was 31·8 years, significantly lower than that for female cases, 36·5 years. With affective psychoses the relationship is reversed; the female cases are more abundant, at least those of early onset. In the same data of Malzberg, male first admissions with manic-depressive psychosis were significantly older than corresponding female cases. Table III shows the details.

TABLE II.—RESIDENT POPULATION ANALYSED ACCORDING TO LENGTH OF TIME SINCE ADMISSION (SEVERALLS MENTAL HOSPITAL)

Type of disorder	First admissions (1934)	0–5 yrs.	5–10 yrs.	10–15 yrs.	15–20 yrs.	20 years+
	%	%	%	%	%	%
Schizophrenia ..	33·3	45·3	53·5	55·0	57·4	69·8
Organic	40·8	32·3	23·4	12·9	8·8	8·0
Manic-depressive	17·5	14·8	13·6	16·2	13·9	7·4
Epileptic	4·3	4·6	6·9	6·8	11·1	2·2
No psychosis (mostly defective)	4·1	3·0	2·6	9·1	8·8	12·6
Total number	463	899	346	309	216	364

2. Биометрическая техника.—*Знание обыкновенной статистики предохраняет от элементарных ошибок и помогает установить важность или незначительность метрических отклонений от нормы среди психиатрических больных. Также и число вариаций может быть более точно определено в ненормальных, чем в нормальных группах. Кроме того, ненормальные реакции сами по себе отличаются большей или меньшей разновидностью, т. е. они или слишком разбросаны или же слишком стереотипны.*

Распознование нормальных или ненормальных реакций может быть основано на единичном количественном измерении, на разнице изменения, или же на сложном измерении, т. е. образец или профиль. Распозновательный подход имеет преимущество над другими методами, так как в таком подходе начальные факторы более конкретны и основаны на известных классах, как то—мужчины и женщины, дети и взрослые, специальные клинические типы и т. д.

3. Генетические анализ.—*Статистические данные могут быть полезны и в изучении генетики, а именно в исчислении многократности народонаселения гена и степени единокровности. Сверх того, соединенные клинические и генетические наблюдения могут обнаружить присутствие новых клинических сущностей.*

RESUMEN.—El artículo presenta un sumario, con ejemplos, de los varios métodos estadísticos que pueden tener una aplicacion específica en la psiquiatría.

(1) *Datos actuarios.*—Para concebír el alcance de las problemas psiquiatricas es de gran servicio la simple acumulación de cálculos seguros sobre las edades de los enfermos, sus diagnosis, duración de detención en hospital o bajo tratamiento para enfermedad psiquiatrica. Son muy caracteristicos la edad y el sexo de incidencia correspondiendo a varios grupos de enfermedades. Tales datos tienen valor en el aprecio de los resultados de experimentos terapéuticos pero métodos especiales se tienen que proyectar, pues no hai un prototipo exacto en la estadística demográfica normal o en los estudios sobre pruebas terapéuticas.

(2) *Técnicas biométricas.*—El entendimiento de los métodos estadísticos corrientes previene los errores elementales y asiste en establecer la significación o no de desviaciónes métricas de la normal que se encuentran en los casos psiquiatricos. Tambien puede ser mucho mas marcado el grado de variaciónes en los grupos anormales que en los normales. Además, las reacciónes anormales pueden ser si mismas caracterizadas por demasiados o de menos variedades, i.e. por dispersar o por estereotipar.

El discernimiento entre la reacción normal y anormal puede ser basado sobre una sola medida cuantitativa, sobre diferencia en variación o sobre una medida compound, i.e. un ejemplar o un perfil. El acercamiento discriminador lleva la ventaja sobre otros metodos que en este los factores iniciales son concretos y basados sobre categorias conocidas como varónes y hembras, niños y adultos, tipos clínicos especiales, etc.

(3) *Análisis genésico.*—Los datos actuarios pueden ser útiles en los estudios genesicos conduciendo a el cálculo de la frequencia de los genes y la proporción de consanguinidad en la población. Además, observaciónes clinicas y genésicas pueden juntas descubrir la existencia de neuvas entidas clinicas.

(1) *Actuarial data.*—It is a standard practice in medicine to inquire into the age and sex of every patient, to ascertain the time of onset of the disease and to record previous attacks. In psychiatry, the onset of symptoms is often very difficult to determine but there are two mitigating circumstances. Since mental illness often lasts many years—or a large part of a lifetime—the exact date of onset is of less importance than the epoch of life in which it commences. Furthermore, in serious illness, which necessitates hospital treatment, exact dates of admission and discharge are capable of being recorded automatically. It is surprising how little use has been made in the scientific study of psychiatry of the simple actuarial material relating to mental illness. Reports of the Board of Control forty or fifty years ago were full of interesting information about the ages of patients admitted to mental institutions but presumably this was thought to be of insufficient value more recently and has been dropped. Especially in his early editions, Stoddart (1926) discussed such statistics at length; few more modern texts, however, give any space to them. The elementary accountancy of numbers of patients under hospital care (or under treatment at clinics) is of great sociological as well as of clinical interest. I propose to cite examples of this and other statistical points in connexion with psychiatric problems and I must apologize if most of them are drawn from my own observations: such examples are naturally most easily available to me.

It is a matter of common knowledge that only a small proportion of the mentally ill or defective persons in the general community are actually certified. The proportion so dealt with depends upon the degree of development of the mental health services. Some years ago I compared statistics from all countries in the world for which figures were available, and came to the conclusion that the amount of attention paid to mental health was inversely proportional to the amount of serious crime (Penrose, 1939). Very roughly, two beds in a mental hospital made one prison cell unnecessary. As prisons cost twice as much as mental hospitals per inmate, there is approximate economical equivalence but social advantage is presumably with the hospital beds.

In the case of mental deficiency much could be learned if we knew the age grouping and intelligence distribution of all institutional cases. Table I shows a rough estimate of the distribution based on surveys of general and institutional populations. One can say that probably one-third of all idiots in the country are under institutional care, one-sixth of all imbeciles but only one-twentieth of all feeble-minded; and of the borderline cases only an extremely small fraction. It is evident that some very strong selective mechanisms determine just which cases shall be cared for and which left in the community. Undoubtedly, those whose families are in poor circumstances contribute an undue proportion of cases and, furthermore, patients with behaviour disorder added to defect are concentrated in the institutional group.

TABLE I.—DEFECTIVES OF ALL TYPES: ESTIMATED NUMBERS IN ENGLAND AND WALES

Grade	Total in general population	Institutional cases	Proportion in institutions
Borderline ..	?	5,000	1/....
Feeble-minded	300,000	15,000	1/20
Imbecile ..	80,000	13,000	1/6
Idiot	20,000	7,000	1/3
Total	400,000	40,000	1/10

Turning to the mentally ill, an elementary example of the value of actuarial data is the difference found in proportions of diagnoses according to whether we consider first admissions or resident populations. The trends are shown in Table II (Duncan *et al.*, 1936). The longer a patient stays in hospital the more likely is he to be a diagnosed schizophrenic, even if he did not start with this diagnosis. In general, diagnosis in psychiatry is so elusive that the age and sex of patients on first admission, which is a very good guide, cannot be neglected. The cases fall naturally into four classes, which have their maximum frequencies in the four double decades 0 to 20, 20 to 40, 40 to 60, 60 to 80. The classes are, mental defect, schizophrenia, affective psychosis and organic psychosis. Fig. 1 (p. 866) shows the relationship of diagnosis and age in 9,821 patients first admitted to the Ontario mental hospitals during the years 1939 to 1942. For simplicity here, epilepsy has been grouped with mental defect and some miscellaneous diagnoses have been included with the organic. Specifying sex gives further information. There are relatively more male cases of early onset and of late onset than female cases, who, in their turn, are more frequent in the central period, 30 years to 50 years. Classification according to both diagnosis and sex helps to explain this phenomenon. Schizophrenia (like mental defect) is more severe in males than in females as shown by its earlier onset in the male sex. Malzberg's (1935) survey of admissions to New York State Mental Hospitals is typical of all large bodies of data in this respect. He found that the mean first admission age for male cases of dementia præcox was 31·8 years, significantly lower than that for female cases, 36·5 years. With affective psychoses the relationship is reversed; the female cases are more abundant, at least those of early onset. In the same data of Malzberg, male first admissions with manic-depressive psychosis were significantly older than corresponding female cases. Table III shows the details.

TABLE II.—RESIDENT POPULATION ANALYSED ACCORDING TO LENGTH OF TIME SINCE ADMISSION (SEVERALLS MENTAL HOSPITAL)

Type of disorder	First admissions (1934)	0–5 yrs.	5–10 yrs.	10–15 yrs.	15–20 yrs.	20 years+
	%	%	%	%	%	%
Schizophrenia ..	33·3	45·3	53·5	55·0	57·4	69·8
Organic	40·8	32·3	23·4	12·9	8·8	8·0
Manic-depressive	17·5	14·8	13·6	16·2	13·9	7·4
Epileptic	4·3	4·6	6·9	6·8	11·1	2·2
No psychosis (mostly defective)	4·1	3·0	2·6	9·1	8·8	12·6
Total number	463	899	346	309	216	364

TABLE III.—FIRST ADMISSION AGES (MALZBERG, 1935)

Diagnosis	Sex	Number of cases	Mean of first admission age in years	Standard deviation of first admission age in years
Dementia Præcox	Male	4,163	31·8	10·5
	Female	3,376	36·5	11·6
Manic-depressive psychosis	Male	1,530	38·3	13·7
	Female	2,316	36·2	12·4

The use of statistics in estimating effects of toxins, drugs or therapeutic procedures has produced a considerable level of accuracy in animal experiments but in medical practice the problem of finding adequate control populations often prevents reliable conclusions from being reached. About 1930, Park suggested a method of assessing the value of pneumonia antisera by making out standard tables of recovery rates in pneumonia, taking into consideration a variety of important points such as age and sex of patient, length of illness, temperature fluctuations, cyanosis, blood picture and so on. Very large numbers of cases are needed in such a control group to match every significant peculiarity of a specially treated case and, in the treatment of mental illness, the problems are even more difficult.

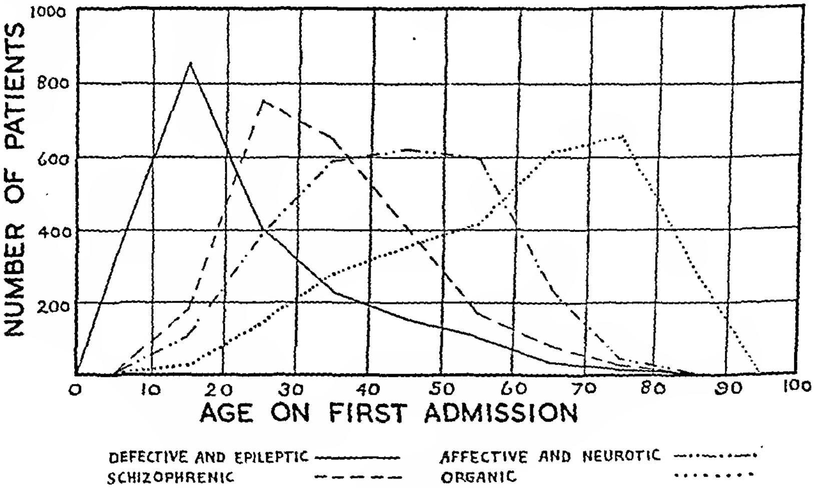


FIG. 1.

In one respect, however, we are lucky, because, as I have tried to demonstrate, age of onset, which is closely correlated with age on first admission, is a good index of diagnosis. We can, if we have good statistical records, find out the chances that a patient, first admitted at any given age, will be found on the books of a mental hospital at any subsequent point in time. The calculation of this chance has no prototype in vital statistics because the patients are frequently discharged and subsequently readmitted—often to a different hospital. Only a central register can take care of this circumstance. Tables which were prepared in the Ontario Department of Health to establish the chances of remaining in hospital for all types of patients (Penrose and Marr, 1943) were, to my mind, extremely interesting. A summary of the most important results is given in Table IV. The method involved one

TABLE IV.—PERCENTAGES OF PATIENTS ON HOSPITAL BOOKS* AFTER A GIVEN LAPSE OF TIME

	Lapse of time since first admission					
	1 year		5 years		25 years	
Age on first admission	Male %	Female %	Male %	Female %	Male %	Female %
0–19	65	76	38	53	28	30
20–39	58	50	32	29	25	27
40–59	50	48	17	24	13	16
60–79	43	66	9	20	1	2
80 +	29	70	0	0	0	0
All ages	52	57	23	30	18	20
All ages—both sexes ..	55		26		19	

*Some patients represented here will have been continuously in hospital all the time since first admission and others readmitted to hospital.

serious omission, in that there was no exact way of allowing for the difference in mortality rate of psychotic and non-psychotic subjects outside the hospital. As they stand, these norms of expected chances of remaining in hospital are, I believe, accurate, but one cannot tell from them, when a patient has not returned after a period of time, whether this is because he has been cured or because he has died. Thus, while comparisons could be made between expected and observed cases in hospital after treatments of various kinds, if a treatment should tend to shorten patients' lives, this would appear on the favourable side of the ledger. Fortunately, examination of known individual cases did not suggest that this was a source of error of any significant magnitude in comparing treated cases with the control population. The comparison of observed and expected numbers of specially treated cases could be made, after separate tables had been compiled for different intervals between first admission and beginning of treatment for both sexes. The types of readings finally obtained are shown in Table V. First admission age, sex, interval between first admission and special treatment and interval since such treatment was observed in each member of the special treatment group (*a*) and was matched in the control group (*b*). The figures indicate clearly that quite good results were obtained after three to four years by shock therapy in cases of psychosis with late onset but no appreciable effect was obtained by all the vast amount of work with coma or convulsion therapy done on the cases of early onset, the majority of whom were diagnosed schizophrenia. Some careful observers have considered these results too pessimistic (Freudenberg, 1947; Mayer-Gross and Slater, 1947). The main point of difference between the method described here and those in general use is the discarding of diagnosis for purposes of matching in favour of unbiased facts about dates and ages of patients.

TABLE V.—CASES TREATED DURING 1939 TO 1941 IN ONTARIO MENTAL HOSPITALS BY COMA OR CONVULSION THERAPY: STATUS IN NOVEMBER 1943

First admission age-group	Number of cases	(*a*) Observed number still on books	(*b*) Expected number still on books	Difference (*a*)−(*b*)
0–19	155	71	71·46	− 0·46
20–29	621	319	330·77	−11·77
30–39	458	197	231·44	−34·44
40–49	226	85	104·44	−19·44
50 and over	140	31	61·29	−30·29
All cases	1600	703	799·40	−96·40

First admission age-group	% of cases	(*a*) Observed % on books	(*b*) Expected % on books	Difference (*a*)−(*b*)
0–19	100·0	45·8	46·1	− 0·3
20–29	100·0	51·4	53·3	− 1·9
30–39	100·0	43·0	50·5	− 7·5
40–49	100·0	37·6	46·2	− 8·6
50 and over	100·0	22·1	43·8	−21·7
All cases	100·0	43·9	50·0	− 6·1

(2) *Biometric techniques.*—The scientific study of mental disorder is partly a matter of recognizing qualities of ideas and of behaviour in patients, which we call pathological. As in other branches of medicine, we also recognize physical disturbances and, in so far as psychiatry is concerned, especially those bodily disturbances which are accompanied by mental changes, e.g. G.P.I., mongolism, hypothyroidism, &c. When the difference between the normal and the pathological is gross, no difficulty is experienced in making decisions but, unfortunately, many signs are only slight and merely give indications of trends. Moreover, one sign is not usually enough to determine the presence of a disease process and we need to add up the evidence from a variety of observations and weigh it before coming to a decision. It is sometimes convenient not to rely upon "all or none" qualitative judgments of presence or absence of signs but to use characters which are capable of being arranged in an ordered series and, in the extreme case, to take actual measurements. Thus, we may estimate the basal metabolism, the blood cholesterol or bromide content or the length of a set of numbers which can be repeated from memory. For example, mental defect is defined as social failure but a main symptom is failure on intelligence tests. The normals and abnormals overlap but, as Pearson first showed, physical measurements give much poorer discrimination.

To distinguish the limits of normal on the basis of distributions is typical of modern statistical teaching and it is of course done by ascertaining the probability against such

TABLE III.—FIRST ADMISSION AGES (MALZBERG, 1935)

Diagnosis	Sex	Number of cases	Mean of first admission age in years	Standard deviation of first admission age in years
Dementia Præcox	Male	4,163	31·8	10·5
	Female	3,376	36·5	11·6
Manic-depressive psychosis	Male	1,530	38·3	13·7
	Female	2,316	36·2	12·4

The use of statistics in estimating effects of toxins, drugs or therapeutic procedures has produced a considerable level of accuracy in animal experiments but in medical practice the problem of finding adequate control populations often prevents reliable conclusions from being reached. About 1930, Park suggested a method of assessing the value of pneumonia antisera by making out standard tables of recovery rates in pneumonia, taking into consideration a variety of important points such as age and sex of patient, length of illness, temperature fluctuations, cyanosis, blood picture and so on. Very large numbers of cases are needed in such a control group to match every significant peculiarity of a specially treated case and, in the treatment of mental illness, the problems are even more difficult.

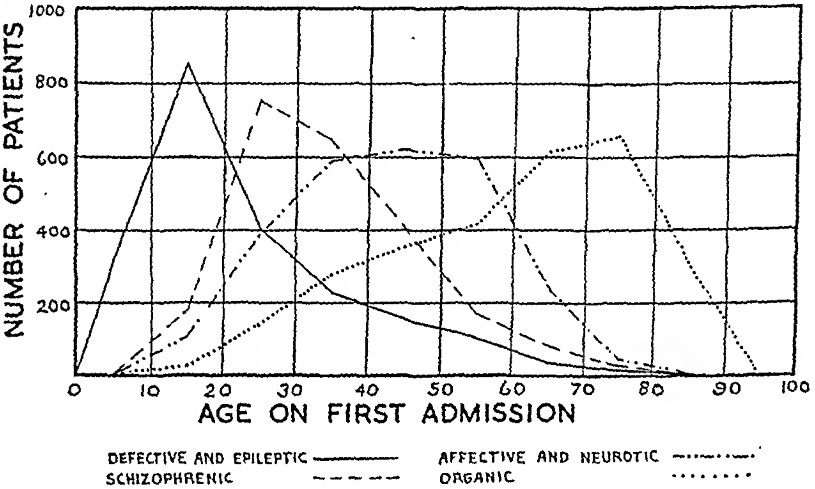


FIG. 1.

In one respect, however, we are lucky, because, as I have tried to demonstrate, age of onset, which is closely correlated with age on first admission, is a good index of diagnosis. We can, if we have good statistical records, find out the chances that a patient, first admitted at any given age, will be found on the books of a mental hospital at any subsequent point in time. The calculation of this chance has no prototype in vital statistics because the patients are frequently discharged and subsequently readmitted—often to a different hospital. Only a central register can take care of this circumstance. Tables which were prepared in the Ontario Department of Health to establish the chances of remaining in hospital for all types of patients (Penrose and Marr, 1943) were, to my mind, extremely interesting. A summary of the most important results is given in Table IV. The method involved one

TABLE IV.—PERCENTAGES OF PATIENTS ON HOSPITAL BOOKS* AFTER A GIVEN LAPSE OF TIME

Age on first admission	Lapse of time since first admission					
	1 year		5 years		25 years	
	Male %	Female %	Male %	Female %	Male %	Female %
0–19	65	76	38	53	28	30
20–39	58	50	32	29	25	27
40–59	50	48	17	24	13	16
60–79	43	66	9	20	1	2
80 +	29	70	0	0	0	0
All ages	52	57	23	30	18	20
All ages—both sexes ..	55		26		19	

---

*Some patients represented here will have been continuously in hospital all the time since first admission and others readmitted to hospital.

serious omission, in that there was no exact way of allowing for the difference in mortality rate of psychotic and non-psychotic subjects outside the hospital. As they stand, these norms of expected chances of remaining in hospital are, I believe, accurate, but one cannot tell from them, when a patient has not returned after a period of time, whether this is because he has been cured or because he has died. Thus, while comparisons could be made between expected and observed cases in hospital after treatments of various kinds, if a treatment should tend to shorten patients' lives, this would appear on the favourable side of the ledger. Fortunately, examination of known individual cases did not suggest that this was a source of error of any significant magnitude in comparing treated cases with the control population. The comparison of observed and expected numbers of specially treated cases could be made, after separate tables had been compiled for different intervals between first admission and beginning of treatment for both sexes. The types of readings finally obtained are shown in Table V. First admission age, sex, interval between first admission and special treatment and interval since such treatment was observed in each member of the special treatment group (*a*) and was matched in the control group (*b*). The figures indicate clearly that quite good results were obtained after three to four years by shock therapy in cases of psychosis with late onset but no appreciable effect was obtained by all the vast amount of work with coma or convulsion therapy done on the cases of early onset, the majority of whom were diagnosed schizophrenia. Some careful observers have considered these results too pessimistic (Freudenberg, 1947; Mayer-Gross and Slater, 1947). The main point of difference between the method described here and those in general use is the discarding of diagnosis for purposes of matching in favour of unbiased facts about dates and ages of patients.

TABLE V.—CASES TREATED DURING 1939 TO 1941 IN ONTARIO MENTAL HOSPITALS BY COMA OR CONVULSION THERAPY: STATUS IN NOVEMBER 1943

First admission age-group	Number of cases	(*a*) Observed number still on books	(*b*) Expected number still on books	Difference (*a*)−(*b*)
0–19	155	71	71·46	− 0·46
20–29	621	319	330·77	−11·77
30–39	458	197	231·44	−34·44
40–49	226	85	104·44	−19·44
50 and over	140	31	61·29	−30·29
All cases	1600	703	799·40	−96·40

First admission age-group	% of cases	(*a*) Observed % on books	(*b*) Expected % on books	Difference (*a*)−(*b*)
0–19	100·0	45·8	46·1	− 0·3
20–29	100·0	51·4	53·3	− 1·9
30–39	100·0	43·0	50·5	− 7·5
40–49	100·0	37·6	46·2	− 8·6
50 and over	100·0	22·1	43·8	−21·7
All cases	100·0	43·9	50·0	− 6·1

(2) *Biometric techniques.*—The scientific study of mental disorder is partly a matter of recognizing qualities of ideas and of behaviour in patients, which we call pathological. As in other branches of medicine, we also recognize physical disturbances and, in so far as psychiatry is concerned, especially those bodily disturbances which are accompanied by mental changes, e.g. G.P.I., mongolism, hypothyroidism, &c. When the difference between the normal and the pathological is gross, no difficulty is experienced in making decisions but, unfortunately, many signs are only slight and merely give indications of trends. Moreover, one sign is not usually enough to determine the presence of a disease process and we need to add up the evidence from a variety of observations and weigh it before coming to a decision. It is sometimes convenient not to rely upon "all or none" qualitative judgments of presence or absence of signs but to use characters which are capable of being arranged in an ordered series and, in the extreme case, to take actual measurements. Thus, we may estimate the basal metabolism, the blood cholesterol or bromide content or the length of a set of numbers which can be repeated from memory. For example, mental defect is defined as social failure but a main symptom is failure on intelligence tests. The normals and abnormals overlap but, as Pearson first showed, physical measurements give much poorer discrimination.

To distinguish the limits of normal on the basis of distributions is typical of modern statistical teaching and it is of course done by ascertaining the probability against such and such a deviation being due to a chance fluctuation. I need not exemplify this point, since the theory of statistical estimation and calculation of sampling error is fully dealt with in standard works. It is perhaps worth noting how necessary it has become for even psychiatrists to have a passing acquaintance with these fundamental principles. Elementary calculations enable the probable significance of the difference in the mean admission ages of males and females in Table III to be established.

I wish, however, to draw attention to some peculiarities common in psychiatric data, which require special care in their statistical treatment and to which few academic statisticians have paid much attention. The problem arises in connexion with certain characteristics of the psychotic state. It was observed by Jung and others that, whereas normally, stimulus words led to reaction words which had a limited degree of variation, abnormal subjects gave bizarre responses, repeated the stimulus word or failed to respond altogether. Kent and Rosanoff (1910) attempted to classify word responses by their improbability and to score unusual words as abnormal. But it is also true that too obvious a reply may be abnormal, e.g. the repetition of the stimulus word. The stereotyped response, due to a tendency to perseveration or whatever it may be called, is just as important as the tendency to extreme dispersion. That is to say, in statistical terms, in mental disorder the variance of the reactions is usually increased but also it may be diminished. Increased variance is well known in the tendency for neurotic children to show "scattering" in intelligence test scores (e.g. the Binet). In reaction time measurements, while it has been shown that many mental illnesses lengthen the time between stimulus and response, extreme anxiety to do the test properly can produce abnormally rapid reactions, which can even precede the expected stimulus. The same statistical picture arises in an even more general form, when we consider the Freudian hypothesis, that repression may give rise either to overreaction or to failure of reaction. These characteristics of the disordered mental state lead to problems of statistical estimation of a very interesting type and, if they are not carefully watched, may cause investigators to neglect important information. For example, on the results of personality tests of the questionnaire variety and even on those with more elaborate techniques like the Rorschach, many abnormal subjects and often just those whom we desire especially to detect, give normal scores. Perhaps some of these scores are just a little *too* normal and this underreaction tendency can rarely be detected by the usual methods of scoring.

To illustrate the point concretely I take an example of a simple test given to a few normal and psychotic subjects. Each subject was required to tap as quickly as possible (for twenty-five seconds) on a metal plate. The taps were electrically recorded on a revolving drum and each hand was given a trial. The scores were plotted as shown in fig. 2 and are summarized in Table VI. Unquestionably the patients as a group were slower than the normals but some were quite within the normal limits. However, the range of speeds among the patients was much wider than among the normals. Each individual record was also analysed for

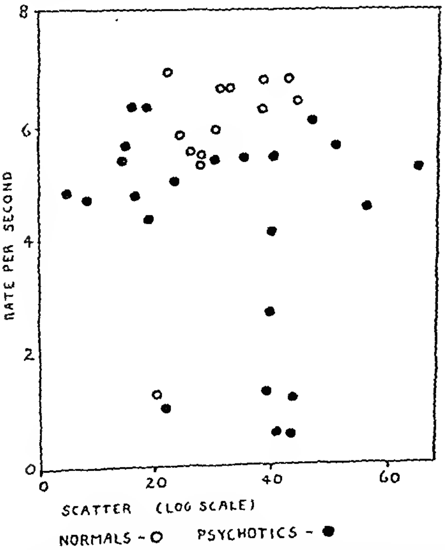


FIG. 2.—Tapping speed. *Unpractised adult subjects.*

TABLE VI.—TAPPING TEST:

NUMBER OF TAPS PER SECOND FOR 25 SECONDS

Group of subjects	Speed, i.e. number of taps per second		Measure of scatter in response	
	Mean	Standard deviation	Mean	Standard deviation
12 normals	6·18	0·57	32·08	6·88
24 psychotics	4·07	1·95	31·04	15·58

(The variability of both the speeds and the scatter is greater in the psychotic group. The mean speeds for normals and psychotics differ significantly.)

irregularity or scatter. Normally, there is a certain amount of irregularity due to fatigue and other causes, which can be estimated by finding the degree of variation from second to second in the ordinary way by a mean square method. When the same analysis was made for abnormals it was found that, though the average amount of scatter was the same as before, the range of scatter was much wider. To obtain the greatest possible diagnostic advantage out of such a test we need a function which will measure the distance in all directions from the centre of the normal group. Thus, records with slow rates and records with too little or too much variation are all suspected of being abnormal. If we try to distinguish between normal and abnormal subjects in such data as these, by ordinary methods, no use can be made of the fact that two groups differ in range. It is, however, easy to devise methods which will do so efficiently (Penrose, 1947).

A great deal of work has been done recently on the analysis of measurements of all kinds in psychiatric work. On the physical side, the stimulus of Kretschmer is still felt. It is now realized, however, that neither the mentally ill nor the normal can be clearly divided into two or more types. The distributions of all measurements or of their combinations tend to be continuous. The present fashion is to search for factors rather than types but analysis by the Spearman-Thurstone method does not necessarily lead to the discovery of factors which are of clinical or genetical interest. As Thomson has pointed out, the factors obtained are determined by the tests and any three tests will produce a general factor of some sort. All the argument about the existence or otherwise of "g" would be avoided if we started with a definition of intelligence as that which normals have and defectives lack. Then each test of intelligence would stand or fall by its ability to discriminate defectives from normals. A good test then can be used with known precision as part of our clinical armoury to diagnose and investigate cases as they arise in practice. From the point of view of research, it is always advisable to proceed from the known to the unknown and, thus, to start with known differences, e.g. between normals and defectives, between the sexes, between normals and neurotics or between different types of diseases. We can then apply the discriminating qualities extracted from these known types to unknown conditions. It is perhaps a good thing that we do not have to rely upon the results of factor analysis for the diagnosis of syphilis.

Terman and Miles (1936) have set up an ingenious test which discriminates quite well between male and female normal reaction types. There are several parts to the test; one part is a "controlled association" test which uses ink blots. Males score significantly more than females if the answers given by normal males are considered to be the correct ones. By applying the same standardized test to any subject we can measure the degree of maleness or femaleness in the reaction. Such tests may have considerable value in psychiatry where homosexual overt or latent tendencies are extremely important in symptomatology. Almost any mental or physical measurement can be used to some degree as a discriminator between different types. For example, the Canadian Army M-test is a battery of 8 sub-tests; picture absurdities, paper form board, mechanical information, arithmetic and verbal tests are included. Normal males did better in some parts of this test and normal females in others. A combination of the weighted scores on four of the sub-tests gave quite a good separation of males and females (Beall, 1945), either by using Fisher's complete solution method or by a simpler method, which reduces a system of any number of measurements to two factors which can be called *size* and *profile*.

Similarly, the M-test, like any mixed battery, could be scored for psychosis *versus* normals by suitable weighting of sub-test scores. The profile of success and failure of mentally ill subjects showed all the well-known features. Tests involving uncritical reproduction of past experience, vocabulary and arithmetic, were fairly well done but absurdities were found very difficult for such subjects to detect (Penrose, 1945). Direct weighting of sub-test scores on the basis of this profile led to a fair discrimination. A *profile* is here defined, for statistical purposes, as any set of weights (applied to test scores expressed in terms of their sigmas) which add up to zero. More critical discrimination can be obtained if the fact is used that the general scoring level in psychotic subjects is usually diminished below the normal. But there are some advantages in considering profile and intelligence level (or size) separately. These are two compound characters which can be used for discriminative purposes separately or in combination. Another type of test, a verbal controlled association test, was tried out in a similar way by Neal (1942). There were 30 items and a complete Fisher solution, such as was used successfully by P. Slater (Bennett and Slater, 1945) on a battery of questionnaires, would have been impracticable. However, scoring level (the size measurement) and profile weighting both gave good differentiation in normal and abnormal subjects and Smith (1947) showed how differences in variances could also be used in combining the two factors.

Discriminative measurements, of course, need not be compound tests like those derived from profiles but can be single measurements like stature, weight, and so on, or ratios and such a deviation being due to a chance fluctuation. I need not exemplify this point, since the theory of statistical estimation and calculation of sampling error is fully dealt with in standard works. It is perhaps worth noting how necessary it has become for even psychiatrists to have a passing acquaintance with these fundamental principles. Elementary calculations enable the probable significance of the difference in the mean admission ages of males and females in Table III to be established.

I wish, however, to draw attention to some peculiarities common in psychiatric data, which require special care in their statistical treatment and to which few academic statisticians have paid much attention. The problem arises in connexion with certain characteristics of the psychotic state. It was observed by Jung and others that, whereas normally, stimulus words led to reaction words which had a limited degree of variation, abnormal subjects gave bizarre responses, repeated the stimulus word or failed to respond altogether. Kent and Rosanoff (1910) attempted to classify word responses by their improbability and to score unusual words as abnormal. But it is also true that too obvious a reply may be abnormal, e.g. the repetition of the stimulus word. The stereotyped response, due to a tendency to perseveration or whatever it may be called, is just as important as the tendency to extreme dispersion. That is to say, in statistical terms, in mental disorder the variance of the reactions is usually increased but also it may be diminished. Increased variance is well known in the tendency for neurotic children to show "scattering" in intelligence test scores (e.g. the Binet). In reaction time measurements, while it has been shown that many mental illnesses lengthen the time between stimulus and response, extreme anxiety to do the test properly can produce abnormally rapid reactions, which can even precede the expected stimulus. The same statistical picture arises in an even more general form, when we consider the Freudian hypothesis, that repression may give rise either to overreaction or to failure of reaction. These characteristics of the disordered mental state lead to problems of statistical estimation of a very interesting type and, if they are not carefully watched, may cause investigators to neglect important information. For example, on the results of personality tests of the questionnaire variety and even on those with more elaborate techniques like the Rorschach, many abnormal subjects and often just those whom we desire especially to detect, give normal scores. Perhaps some of these scores are just a little *too* normal and this underreaction tendency can rarely be detected by the usual methods of scoring.

To illustrate the point concretely I take an example of a simple test given to a few normal and psychotic subjects. Each subject was required to tap as quickly as possible (for twenty-five seconds) on a metal plate. The taps were electrically recorded on a revolving drum and each hand was given a trial. The scores were plotted as shown in fig. 2 and are summarized in Table VI. Unquestionably the patients as a group were slower than the normals but some were quite within the normal limits. However, the range of speeds among the patients was much wider than among the normals. Each individual record was also analysed for

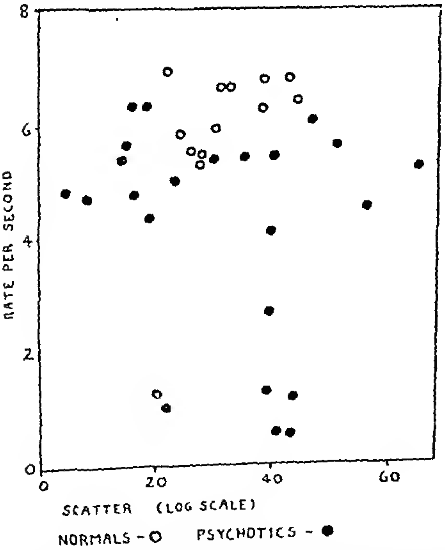


FIG. 2.—Tapping speed. Unpractised adult subjects.

TABLE VI.—TAPPING TEST:

NUMBER OF TAPS PER SECOND FOR 25 SECONDS

	Speed, i.e. number of taps per second		Measure of scatter in response	
Group of subjects	Mean	Standard deviation	Mean	Standard deviation
12 normals	6·18	0·57	32·08	6·88
24 psychotics	4·07	1·95	31·04	15·58

(The variability of both the speeds and the scatter is greater in the psychotic group. The mean speeds for normals and psychotics differ significantly.)

Section of Proctology

President—A. Hedley Whyte, D.S.O., T.D., M.S., F.R.C.S.

[*March* 12, 1947, *concluded*]

Specimen of Colon Removed on Account of Severe Pyoderma from a Long-Standing Case of Chronic Ulcerative Colitis.—Rupert S. Corbett, M.Ch.

The specimen was removed from a female aged 46, suffering for twelve years from chronic ulcerative colitis.

On account of recurrent attacks of colicky pain, with vomiting, loss of weight associated with fever and a reduction in the hæmoglobin to 42%, a terminal ileostomy was performed. This led to a very great improvement in her general health; she could eat anything and the rectal discharge diminished considerably. Weight increased and the Hb went up to 66%.

It was noted that the rectal discharge persisted from 2 to 4 oz. daily and was offensive mucopus. In addition she developed large superficial areas of ulceration on the thigh and calf of the right lower extremity. The skin condition was diagnosed as pyoderma.

It was decided to perform a subtotal colectomy. This has resulted in a very great improvement to her general health and no recurrence of the skin lesion.

I wish to emphasize the importance of this skin complication as an indication for colectomy. Other authorities have referred to the common association of erythema nodosum which often breaks down to the condition of pyoderma gangrenosum.

The X-ray film shows the condition of the colon prior to excision and the photograph shows the condition of the specimen after removal.

Pathological report (Dr. C. E. Dukes).—Colon removed by right subtotal colectomy 21.11.46.

The specimen consisted of the cæcum, ascending colon, transverse and descending colon and also about 3 in. (7·6 cm.) of the ileum. The whole colon was much thickened and contracted down and embedded in tough fibrous fatty tissue. Dissection showed the

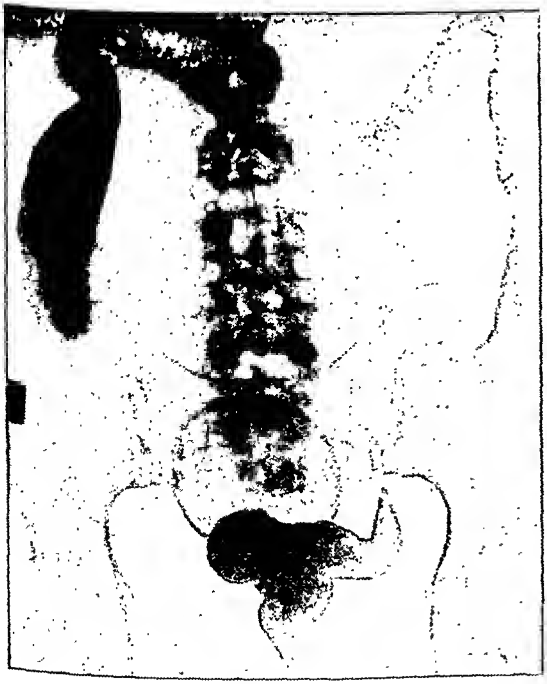


Fig. 1.

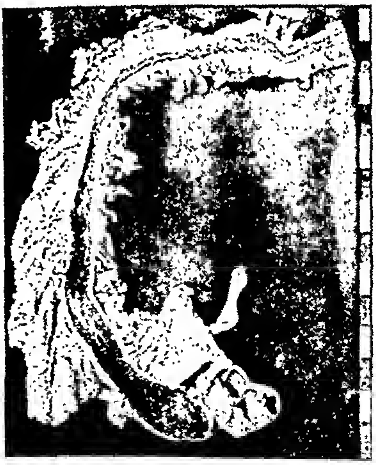


Fig. 2.

Fig. 1.—Barium enema prior to colectomy, November 1946. (Note calcified fibroid of the uterus.)

Fig. 2.—Specimen, inside view.

like cephalic index or stature divided by chest diameter (Rees and Eysenck, 1945). Having ascertained that they differentiate two groups well, we can then measure any person and inquire to which end of the scale he has the greater affinity. When a male–female test has been set up, we can test a patient and find whether he deviates in any direction from the normal for his sex. Very tentative experiments with the sex profile of the M-test, used as a discriminant between males and females, gave somewhat surprising results. This led me to a theory which I should like to see tested further. It seems that schizophrenics are fundamentally too feminine. Looked at in another way, cases of relatively early onset have intersexual tendency and those of late onset perhaps normal sexuality or supersexual tendency.

(3) *Genetical analysis.*—In conclusion I would like to draw attention to the value of statistical inquiry in the elucidation of the genetical background of psychiatric phenomena. With genetical characters it is of the utmost interest to know their frequencies in the population, since different frequencies involve different properties. It is desirable to know the frequency of cases of Huntington's chorea, for example, and, in addition, subsequent inquiry, case by case, could elicit how many cases were sporadic and in how many cases a parent was affected. From such data an estimate of mutation frequency could ultimately be made.

Diseases due to rare recessive genes can be detected by finding an increased consanguinity rate in the patients' parents. Inquiries have been carried out by Bell (1940) on data from general hospital admissions and by Munro (1938) on mental hospital admissions. Among the mentally defective patients the incidence of consanguinity in parents is particularly illuminating and indicates that some types of cerebral diplegia and microcephaly are due to single recessive genes (Duff and Dingee, 1941).

As previously mentioned, an objection to the method of factor analysis is that the entities which are deduced do not necessarily agree with clinical or genetical factors. Having established a factor, one can, of course, test it genetically by examining families. It is methodologically much more direct first to measure the same trait or set of traits in sibs or other relations and to find out by genetical analysis which traits are likely to be of significance. In its most elementary form the method would involve finding how far disease types are constant in different members of the same family. It would be useful to take, for example, instead of a random sample of men, a random sample of brothers. Genetical likeness, which can be observed in persons who have blood relationship, can be used as a means of grouping disease entities in psychiatry. Genetical differences are factors which should be used as the basis of discrimination between types.

REFERENCES

BEALL, G. (1945) *Psychometrica,* **10,** 205.
BELL, J. (1940) *Ann. Eugen.,* **10,** 370
BENNETT, E., and SLATER, P. (1945) *Brit. J. med. Psychol.,* **20,** 271.
DUFF, P. B. E., and DINGEE, R. W. (1941) *Amer. J. ment Def.,* **46,** 21.
DUNCAN, A. G., PENROSE, L. S., and TURNBULL, R. G. (1936) *J. Neurol. Psychopath.,* **63,** 225.
EYSENCK, H. J. (1944) *J. Ment. Sci.,* **90,** 851.
FREUDENBERG, R. K. (1947) *J. ment. Sci.,* **93,** 9.
KENT, G. H., and ROSANOFF, A. J. (1910) *Amer. J. Insan.,* **67,** 37 and 317.
MALZBERG, B. (1935) *Ment. Hyg.,* **19,** 449.
MAYER-GROSS, W. (1947) (Discussion) *J. ment. Sci.,* **93,** 26.
MUNRO, T. A. (1938) *J. ment. Sci.,* **84,** 708.
NEAL, L. E. (1942) A Clinical Study with a Verbal Classification Test. University of Toronto, Ph.D. Thesis.
PENROSE, L. S. (1939) *Brit. J. med. Psychol.,* **18,** 1.
——, and MARR, W. B. (1943) *J. Ment. Sci.,* **89,** 374.
—— (1945) *Bull. Canad. Psychol. Ass.,* **5,** 37.
—— (1945) *Amer. J. Psychiat.,* **101,** 810.
—— (1947) *Ann. Eugen.,* **13,** 228.
REES, W. L., and EYSENCK, H. J. (1945) *J. ment. Sci.,* **91,** 8.
SMITH, C. A. B. (1947) *Ann. Eugen.,* **13,** 272.
STODDART, W. B. (1926) Mind and Its Disorders. 5th Ed., London.
TERMAN, L. M., and MILES, C. C. (1936) Sex and Personality. N.Y.

Section of Proctology

President—A. Hedley Whyte, D.S.O., T.D., M.S., F.R.C.S.

[*March* 12, 1947, *concluded*]

Specimen of Colon Removed on Account of Severe Pyoderma from a Long-Standing Case of Chronic Ulcerative Colitis.—Rupert S. Corbett, M.Ch.

The specimen was removed from a female aged 46, suffering for twelve years from chronic ulcerative colitis.

On account of recurrent attacks of colicky pain, with vomiting, loss of weight associated with fever and a reduction in the hæmoglobin to 42%, a terminal ileostomy was performed. This led to a very great improvement in her general health; she could eat anything and the rectal discharge diminished considerably. Weight increased and the Hb went up to 66%.

It was noted that the rectal discharge persisted from 2 to 4 oz. daily and was offensive mucopus. In addition she developed large superficial areas of ulceration on the thigh and calf of the right lower extremity. The skin condition was diagnosed as pyoderma.

It was decided to perform a subtotal colectomy. This has resulted in a very great improvement to her general health and no recurrence of the skin lesion.

I wish to emphasize the importance of this skin complication as an indication for colectomy. Other authorities have referred to the common association of erythema nodosum which often breaks down to the condition of pyoderma gangrenosum.

The X-ray film shows the condition of the colon prior to excision and the photograph shows the condition of the specimen after removal.

Pathological report (Dr. C. E. Dukes).—Colon removed by right subtotal colectomy 21.11.46.

The specimen consisted of the cæcum, ascending colon, transverse and descending colon and also about 3 in. (7·6 cm.) of the ileum. The whole colon was much thickened and contracted down and embedded in tough fibrous fatty tissue. Dissection showed the

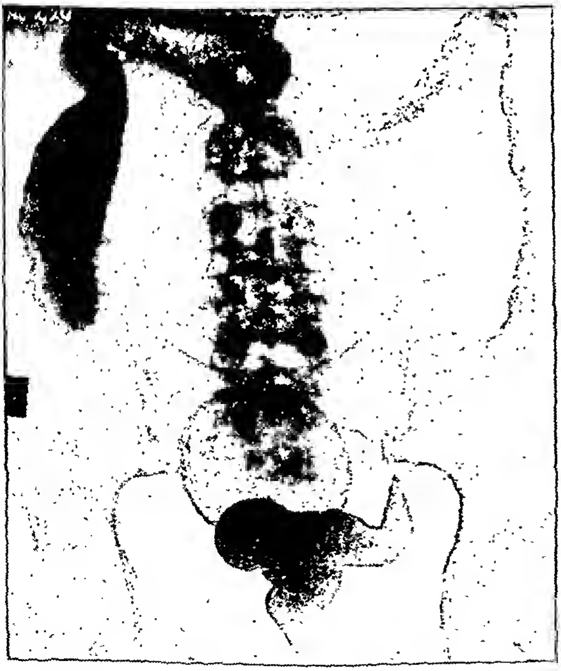


Fig. 1.

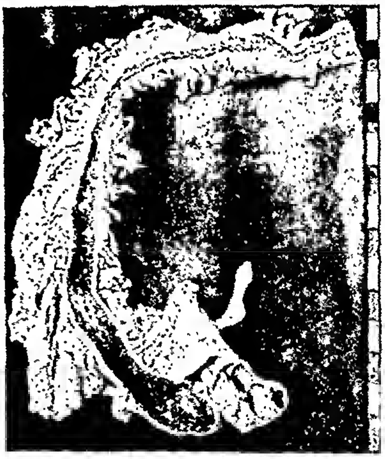


Fig. 2.

Fig. 1.—Barium enema prior to colectomy, November 1946. (Note calcified fibroid of the uterus.)

Fig. 2.—Specimen, inside view.

mucosal surface of the colon to be dark brown in colour and covered with ridges and small polypoid tumours, mostly about the size of a pinhead. These ceased abruptly at the ileocæcal valve and the mucous surface of the small intestine was normal in appearance.

Microscopic structure.—Sections show extensive ulceration of the mucous membrane with only small surviving patches of mucosa. In the bare areas the submucosa is occupied by very vascular granulation tissue containing large numbers of lymphoid cells, plasma cells and eosinophils. In some regions there appears to be hyperplasia of the lymphoid tissue and the dark colour is due to blood pigment, of which there is a considerable quantity in the submucosa. There is no sign of any form of malignancy.

Associated Carcinoma of Colon and Rectum

Report of Two Cases

By Frank Forty, M.B., B.S., F.R.C.S.
(*Surgeon, Redhill County Hospital, Edgware*)

The occurrence of multiple primary carcinomata is not one of the great rarities of surgical pathology.

Few such tumours, however, have been recorded as affecting exclusively the colon and rectum. The majority occur in unrelated systems or organs.

Cokkinis, reviewing the literature in 1934, found that only 29 authentic cases of multiple tumours confined to the large bowel had been recorded up till that date.

Norbury (1931), in his Presidential Address to this Section on "Multiple Primary Malignant Growths, with Special Reference to the Colon and Rectum", reported several cases and stressed the practical importance of a thorough search for multiple tumours before planning any radical operation, or the placing of a colostomy. He also discussed the difficult question of the ætiology of multiple tumours, with regard to the possibilities of their arising independently, in areas of diffuse polyposis, or as implants of detached portions of one growth into another part of the bowel. Consideration was also given to the possibility that a familial or hereditary susceptibility might favour the development of multiple carcinomata, but this influence would not appear to operate with any greater frequency in cases of multiple, than in those of single primary malignant growths.

Case I.—Mrs. E. T., aged 61, was first seen in May 1945.

History.—Bleeding *per rectum* on defæcation for past three months. Bowels regular but with passage of excessive flatus. No mucous discharge. No abdominal pain. Some loss of weight.

Examination.—A carcinoma was palpable in the upper third of the rectum. *Per abdomen*, a mass was palpable in the right upper quadrant which moved up and down with respiration and which was suggestive of an enlargement of the liver. This was thought to be probably due to metastases from the carcinoma in her rectum.

First operation (5.6.45).—*Exploration*: The mass which had been felt on examination of the abdomen was found to be an annular carcinoma in the ascending colon 1½ in. (3·8 cm.) beyond the ileocæcal junction. There were no local attachments and no glandular metastases, nor secondary deposits in the liver or elsewhere. The presence of a mobile carcinomatous ulcer at the rectosigmoid junction was confirmed. There was no gross intestinal obstruction.

Operative procedure: Right hemicolectomy for adenocarcinoma of cæcum, completed by the Paul-Mikulicz method. Post-operative progress uneventful.

Second operation (10.7.45).—One-stage abdomino-perineal excision of the rectum for adenocarcinoma of rectosigmoid junction.

Post-operative progress again uneventful until signs of small-gut obstruction developed on the tenth day.

Third operation (23.7.45).—The abdomen was reopened and two narrow peritoneal bands, associated with the last parietal incision, were found obstructing a loop of small intestine, and were easily divided.

Although very ill at this time the patient made a good recovery.

On October 10 a small polypus was found presenting at the stoma of the terminal colostomy and excised. Microscopically, this showed a columnar-cell adenocarcinoma.

Fourth operation (16.4.46)—*Extraperitoneal closure of ileocolostomy.* The patient was finally discharged from hospital on May 3, 1946, in good health, and has remained well and free from recurrence.

Case II.—Mrs. C. W., aged 38, was admitted to hospital on July 31, 1943.

History.—Bleeding from rectum on the day before admission, preceded by slight pain "like wind".

Past history.—No previous bowel symptoms nor any previous ill-health.

On examination.—Small hard swelling below right costal margin. No other physical signs.

Investigation.—Barium enema—large filling defect at hepatic flexure suggestive of carcinoma.

First operotion (31.8.43).—*Findings*: Annular carcinoma at right side of transverse colon. Mobile. No secondaries. *Procedure*: Excision by Paul-Mikulicz method. *Microscopical report*: Adenocarcinoma of colon.

Second operation (24.10.44).—Extraperitoneal closure of colostomy. A hard nodule excised from the abdominal wall just above the colostomy showed adenocarcinoma.

First readmission (14.5.45).—*History*: Abdominal enlargement and discomfort for three months. Vaginal discharge three weeks.

On exomination: General condition good. Abdomen—large elastic swelling arising out of pelvis nearly to umbilicus. No ascites. *Per vaginam*—cervix displaced forwards. Mass filling pouch of Douglas continuous with abdominal swelling.

Third operotion (16.5.45) (Mr. E. ap I. Rosser).—*Findings*: Bilateral papilliferous cysts of both ovaries. *Procedure*: Subtotal hysterectomy with removal of both ovaries. At this laparotomy the colon showed no recurrence of growth and the abdomen was free from adhesions. *Microscopical examination of ovarion tumours*: "Section shows secondary carcinoma. Structure would fit well with colonic primary."

Second readmission (12.1.47).—*History*: Bleeding *per rectum*, onset two weeks previously. Bowels rather constipated.

On exominotion: Hard nodule present in the lower mid-line laparotomy scar. No intraperitoneal mass palpable. *Per rectum* indurated ulcer with raised edges on left anterior wall.

Investigations: Barium enema ascended to cæcum without delay or difficulty. Insufflation revealed no soft tissue masses. No neoplasm was detected. Sigmoidoscopy revealed a low sessile papillomatous ulcer on the anterior wall of the rectum situated about 4 or 5 in. (10 or 12·5 cm.) from the anus.

Fourth operotion (30.1.47).—*Exploration*: Liver contained no secondaries. No primary or secondary growth discovered in abdominal cavity except for a small nodule in the omentum which was removed. There were several enlarged glands in the pelvic mesocolon and subperitoneal growth was spreading from the rectum along the bottom of the pouch of Douglas, causing some fixation to the left pelvic wall.

Procedure: One-stage abdomino-perineal excision of rectum. A nodule of growth was also removed from the region of the right round ligament and the portion of the mid-line scar containing a nodule of recurrent growth was excised.

Specimen: A papillomatous ulcer, 1½ in. (3·8 cm.) in diameter, 5 in. (12·5 cm.) above the anus, with massive invasion of perirectal tissues.

Microscopical examination: Adenocarcinoma of rectum. Omentum, abdominal wall and right round ligament all show secondary adenocarcinoma. Post-operative progress uneventful.

DISCUSSION

A few points of general interest or significance from the case-histories of these two patients invite comment.

From the practical aspect, Case I exemplifies the point stressed by Norbury in his Presidential Address and by many other writers, namely the importance of suspecting, and searching for, other primary growths when one has been discovered.

The palpable tumour in the right side of the abdomen did somewhat closely simulate an enlargement of the liver, and it would have been unfortunate if this assumption had been accepted without verification.

Secondly, the completion of the right hemicolectomy by a Paul-Mikulicz procedure appeared particularly appropriate in the presence of a second carcinoma at the rectosigmoid junction, which, as a potential cause of obstruction, might have seriously added to the risks of an immediate ileocolic anastomosis.

Furthermore, the temporary ileocolostomy served the useful purpose of isolating and decompressing the distal colon and rectum as a preliminary to the abdomino-perineal excision.

From the theoretical point of view, a tentative opinion that, in both cases, the associated carcinoma in the rectum arose as an implant of a detached fragment from the colonic growth is suggested by the following evidence:

(1) In neither of these patients was there a generalized polyposis. The growths in both excised rectums were solitary; in both cases, palpation of the colon at laparotomy revealed no polypi; and in the second case, a barium enema with air contrast films, specially done to reveal possible multiple polypi, gave a negative result.

(2) The adenocarcinomatous polypus, which formed at the stoma of the left iliac colostomy in Case I, was evidently an implant from the growth in the ascending colon. A similar implant in the rectum therefore seems a likely explanation of the origin of the carcinoma in this situation.

(3) In Case II, the fact that rather profuse hæmorrhage was the first symptom of both the colonic and rectal carcinomata may be an indication of a similarity in the type of growth

and, furthermore, the occurrence of implants in the abdominal wall after each of the first two laparotomies suggests a particular proneness to this manner of spread.

On the basis of these assumptions, the rectal carcinoma would be readily explained as an implant derived from the growth at the hepatic flexure. This, however, implies a very slow rate of growth of the rectal carcinoma in view of the lapse of three years and four months between removal of the colonic tumour and the first appearance of rectal symptoms.

REFERENCES

COKKINIS, A. J. (1934) *Brit. J. Surg.*, **21**, 570. NORBURY, L. (1931) *Proc. R. Soc. Med.*, **24**, 198.

Carcinoma of the Cæcum associated with Carcinoid Tumour of the Small Intestine.—C. NAUNTON MORGAN, F.R.C.S.

S. B., male, aged 65. Musician.

Attended St. Mark's Hospital, complaining of rectal bleeding for years.

On examination.—An ill-looking man; mucous membranes pale; smooth tongue with atrophy of the mucosa. Chest: poor expansion; fine and coarse rhonchi over both lungs. B.P. 80/60 mm.Hg. Abdomen: a large, tender, hard and irregular mass was found in the right iliac fossa, which appeared to be slightly fixed. Rectum showed large third degree internal hæmorrhoids which would account for the bleeding. Sigmoidoscopy to 25 cm. revealed nothing abnormal. Diagnosis: Carcinoma of the cæcum.

Barium enema suggested that the abdominal mass was probably an appendix abscess, there being no definite evidence of a new growth. Hæmoglobin was found to be 66% and white blood-count 13,000 (polymorphonuclear leucocytosis). Patient ran a swinging temperature up to 102/103° F. (38·9/39·5° C.) for the first week and during that time he was given 3 pints (1·7 litres) of blood and one pint (0·57 litre) of serum. Hæmoglobin now was 70%.

For ten pre-operative days he was given phthalylsulphathiazole 10 grammes daily, and his temperature settled soon after its commencement.

Operation was performed twelve days after admission under spinal anæsthesia and continuous drip pentothal. The abdomen was opened by a long right oblique incision and a large mobile carcinoma was found in the cæcum, there being one large palpable gland in the mesentery of the small intestine.

On routine exploration of the abdomen the liver was found to be free of any palpable deposit, but a small hard contracting mass was palpated in the small intestine, which on delivery was found to be an ileal intussusception actually developing. After reduction, a small puckered hard mass was felt in the wall of the ileum and there was a hard gland about 3 in. (7·6 cm.) away in the mesentery. This second growth was thought to be another carcinoma. The whole of the small intestine was examined for other tumours but none was found. The tumour was situated approximately 6 ft. (183 cm.) from the ileocæcal valve.

A right hemicolectomy including approximately 6 ft. of ileum with its mesentery was performed; the apex of the excised mesenteric field being about 1 in. (2·5 cm.) below the duodenum.

The proximal end of the ileum was closed and also the end of the colon just distal to the hepatic angle. A side-to-side anastomosis was performed and the mesenteric defect repaired. The retroperitoneal area in the right loin was drained with Penrose drains. The patient made an uninterrupted recovery and, fifteen days later, his hæmorrhoids were ligatured and excised.

Pathologist's report (21.2.47) (Dr. C. E. Dukes).—*Gross characters.*—The specimen consisted of the cæcum, ascending colon and 9 ft. (2·75 m.) of small intestine. A huge fungating tumour completely encircled the ileocæcal valve and protruded into the cæcum (A). A hard nodule was found in the small intestine causing some constriction of the lumen. This was situated about 5 ft. (152 cm.) from the ileocæcal valve (fig. 1, B).

Microscopic structure.—The growth in the cæcum is an adenocarcinoma of a low grade of malignancy. The tumour in the small intestine is a carcinoid tumour.

Methods of spread.—(1) *By direct continuity*: The cæcal growth had spread into the pericolic fat to a moderate extent. The carcinoid tumour had begun to invade the muscle coat. (2) *Venous spread*: There was no sign of venous spread. (3) *Lymphatic spread*: The glands from the ileocæcal angle were all free from metastases (fifteen glands examined) but of five glands removed from the mesentery of the small intestine in the vicinity of the carcinoid tumour three contained metastases from this growth (fig. 2).

Classification.—Carcinoid tumour of the small intestine with three lymphatic metastases associated with adenocarcinoma of the cæcum free from metastases.

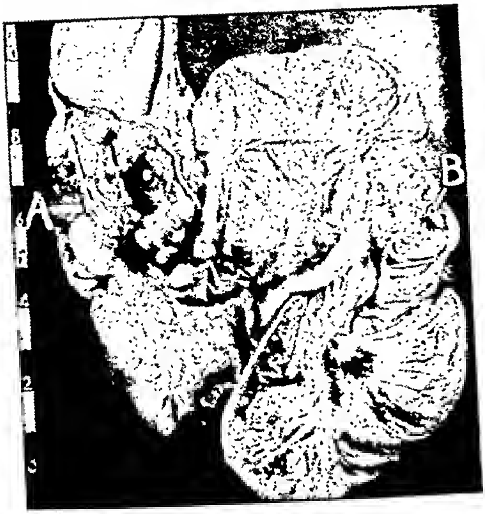


FIG. 1.

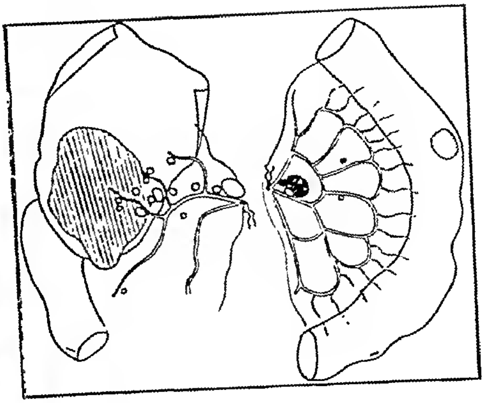


FIG. 2.

The association of a carcinoma with a carcinoid tumour is a very rare occurrence. Carcinoid tumours of the small intestine metastasize more frequently than those of the appendix.

Carcinoma of the Rectum with a Single Secondary in the Liver. Synchronous Combined Excision and Left Hepatectomy.—O. V. LLOYD-DAVIES, M.S.

F. T., male, aged 50.

He attended St. Mark's Hospital in June 1943 with a large carcinoma of the rectum.

At operation 30.6.43 a large single secondary was found in the left lobe of the liver, the right lobe being apparently free from metastases; the primary growth was locally operable and a synchronous combined excision was performed. The rectal growth specimen was classified as a C1 case, only two out of eighteen glands being involved, and from that aspect it was considered that the man had a reasonable chance of a five-year cure.

In the hope that the deposit in the left lobe of the liver might be the only one the left lobe was removed three weeks later 21.7.43 (fig. 1).

The patient made an uninterrupted recovery and returned to his work as a farm labourer in Lincolnshire. On August 26, 1945, he developed an attack of acute intestinal obstruction; he was admitted to

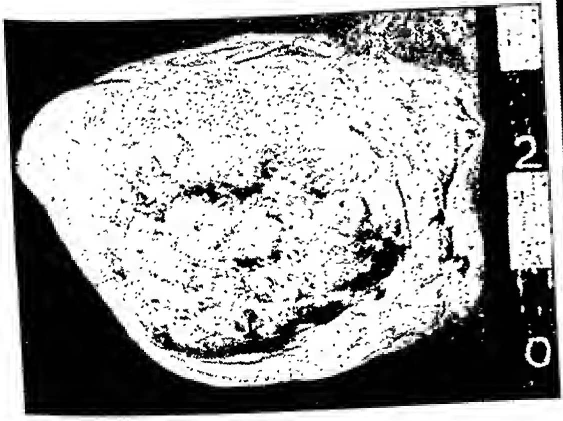


FIG. 1.

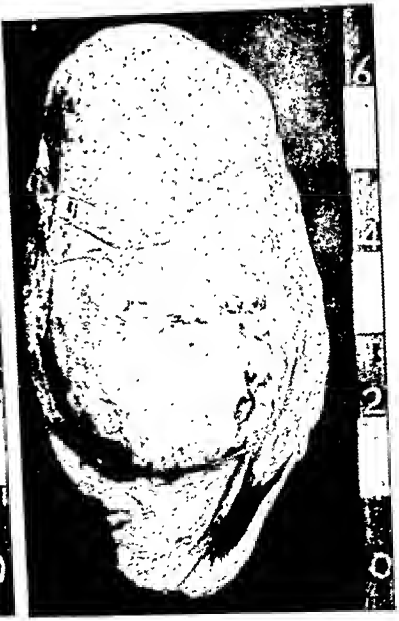


FIG. 2.

his local hospital. Unfortunately the assumption was made that the obstruction was probably due to secondary deposits and there was a forty-eight-hour delay before operation.

At operation it was found that a loop of the small intestine had become adherent to a Meckel's diverticulum; this was relieved, but the patient did not recover and died two days later. At post-mortem no evidence of any other secondaries could be found.

Fig. 2 is another case of a single secondary in the left lobe of the liver removed in June 1946 three and a half years after a resection for a carcinoma of the colon. The progress of this case is being watched with interest.

Partial Hepatectomy and Right Hemicolectomy for Carcinoma of the Hepatic Flexure of the Colon.—RONALD W. RAVEN, O.B.E., F.R.C.S.

Male, aged 38, was admitted to the Royal Cancer Hospital with symptoms extending over one year. Two months before admission another surgeon performed an exploratory laparotomy and found a carcinoma of the hepatic flexure of the colon invading extensively the right lobe of the liver. This was considered inoperable and a palliative ileo-transverse colostomy was performed. The patient's condition was deteriorating rapidly, he was wasted and had severe secondary anæmia—R.B.C. 1,900,000 per c.mm., Hb 28 %. The patient and his wife urged that an attempt should be made to eradicate the tumour and after careful preparation, including the transfusion of large amounts of blood, operation was performed. A large part of the right lobe of the liver, including the gall-bladder and the right half of the colon, was excised. No evidence of secondary carcinoma, apart from the liver extension, was found. Patient made an excellent recovery from the operation.

(A full report of this case appeared in the *British Medical Journal*, 1947 (ii), 249.)

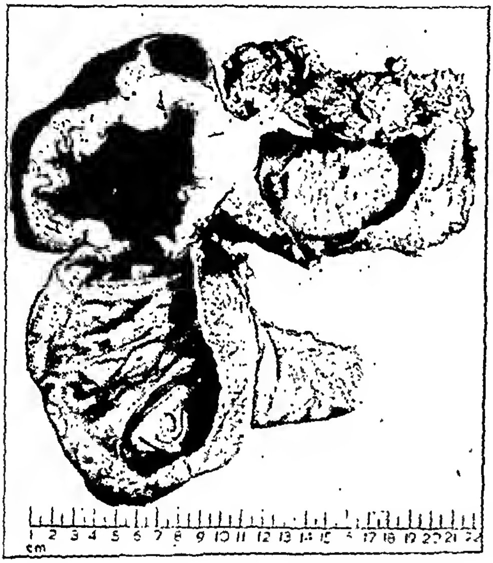


FIG. 1.
Specimen removed at operation showing a part of the right lobe of the liver, gall-bladder and right half of the colon. A large carcinoma of the hepatic flexure of the colon is invading extensively the right lobe of the liver.

[*May* 14, 1947]

DISCUSSION ON
CONGENITAL ANOMALIES OF THE ANORECTAL REGION

Professor John Kirk: *A résumé of the developmental anatomy of the rectum and anal canal.*—The portion of the embryonic gut supplied by the inferior mesenteric artery extends from the distal part of the transverse colon to the junction of the upper two-thirds with the lower third of the anal canal and is termed the "hind-gut". At an early stage it gives off a ventral diverticulum, the allantois, which, passing forwards and upwards into the umbilical stalk, carries with it the two allantoic vessels which will become the umbilical arteries of the placenta. Immediately proximal to the base of the allantois two lateral ridges form on the inner surface of the gut wall and by meeting and fusing in the mid-line form a urorectal septum. This extends caudalwards in a coronal plane and divides the gut-tube at first partially, but finally completely, into a ventral (urogenital) and a dorsal (rectal) compartment.

The genital ducts and the ureters retain their connexion with the urogenital compartment and behind it are embedded in the septum. At first both compartments are shut off from the surface by the cloacal membrane. On the external aspect of this two shallow depressions are discernible; the anterior of these represents the future urogenital cleft and the posterior one (the proctodæum) is destined to form the lower half-inch of the anal canal.

In the eighth week the membrane breaks down and the two passages open on the perineum. They are separated by a condensation of mesoderm, the perineal body, which forms at the point where the septum first makes contact with the membrane. The ectodermal proctodæum is thus brought into continuity with the entodermal gut-tube and the junctional zone becomes a critical landmark in the anatomy, physiology and pathology of the anal canal. Should the anal membrane fail to break down, a form of imperforate anus results.

Fate of the urorectal septum.—The septum is at first solid mesoderm but later becomes excavated by an extension into it of the cœlomic (peritoneal) cavity. Thus is formed the rectovesical pouch in the male, containing in its anterior wall the derivatives of the Wolffian ducts—the vasa deferentia and vesiculæ seminales—as well as the prostate and bladder. In the female, the pouch is further divided by the derivatives of the Müllerian ducts—the uterus, tubes and vaginal canal. The broad ligaments with their parametric tissue are the remains of the urorectal septum itself. In the female there is thus formed both a uterovesical and a uterorectal pouch. At the bottom of the latter the recto-anal flexure is in close contact with the vaginal wall, and beyond it the vaginal and anal canals are separated only by the perineal body.

In the male at birth the rectovesical pouch extends to the perineal body on a level with the apex of the prostate and base of the perineal membrane (triangular ligament). Later, however, this peritoneal pouch is obliterated by the adhesion of its walls. A double sheet of fascia is all that remains (the fascia of Denonvilliers) to separate the prostate, seminal vesicles, and trigone of the bladder in front from the ampulla of the rectum behind.

It is not surprising, therefore, that the commonest site of a congenital communication between the rectum and the urogenital passage, due to a defect in the septum, is found, in the male, to lie in the prostatic urethra just distal to the uterus masculinus, and in the female at a corresponding point, i.e. in the floor of the vestibule just external to the hymen.

In those rare cases where the whole of the rectum as well as the anal canal is absent, the defect is obviously due to an abnormal growth of the urorectal septum which, instead of producing a partition, proceeds to fill up and obliterate the dorsal compartment of the gut cavity and only the patent urogenital sinus remains.

Normally a small and temporary diverticulum of the rectal compartment forms just above and behind the cloacal membrane. This is the post-anal gut. It soon disintegrates and disappears but some remnant may remain to give rise to a dermoid tumour in the anococcygeal region.

PRACTICAL CONSIDERATIONS

The anorectal junction in the adult of both sexes is approximately 1½ in. (3·8 cm.) from the anus and is clearly identified as the point where the ampulla of the rectum suddenly narrows and takes a knuckle-bend downwards and backwards to form the anal canal. Here the puborectalis fibres of the pubo-coccygeus muscle form a sling which loops round the gut on its posterior and lateral aspects to make an anorectal ring of great functional value. The fibres of the iliococcygeus, descending from the lateral pelvic wall, undercut this part of the levator ani and pass downwards alongside the gut as far as the peri-anal skin. *En route* these fibres mingle with the longitudinal coat of the bowel and with the internal and external sphincter muscles. The upper two-thirds of the anal canal is true gut lined by entoderm; the lower third (not more than ½ in. (1·3 cm.) long in the adult) is formed from the proctodæum and its mucous membrane is, therefore, ectodermal in origin.

At the junction of these two zones the columnar epithelium of the one shades off into the stratified squamous epithelium of the other, and the area has been aptly termed the "pecten" or "pectinate line" because its upper limit is the line of the anal valves found at the distal ends of the grooves lying between the anal columns of Morgagni. These columns and grooves are not to be confused with the longitudinal folds and furrows often seen in the lower cutaneous portion of the canal and which correspond to the territory of the superficial part of the external sphincter muscle. The columns of Morgagni are frequently, but erroneously, referred to as "rectal" but they are truly anal in position and, moreover, were originally described as such ("ani columnæ") by Morgagni in 1741.

Just distal to the corrugated line of valvules is the mucocutaneous junction indicated to the naked-eye by the "white line" of John Hilton. In the living subject the line is more often bluish-pink in colour and is best seen in the dark races.

Here in the early embryo was attached the cloacal membrane and here is the boundary line between the splanchnic and somatic territories of the anal canal. Above the pecten the smooth involuntary internal sphincter grips the canal and the nerve supply of the gut, both motor and sensory, belongs to the autonomic system and therefore has a high threshold for pain, touch and temperature stimuli. Its lymphatic drainage is intrapelvic.

his local hospital. Unfortunately the assumption was made that the obstruction was probably due to secondary deposits and there was a forty-eight-hour delay before operation.

At operation it was found that a loop of the small intestine had become adherent to a Meckel's diverticulum; this was relieved, but the patient did not recover and died two days later. At post-mortem no evidence of any other secondaries could be found.

Fig. 2 is another case of a single secondary in the left lobe of the liver removed in June 1946 three and a half years after a resection for a carcinoma of the colon. The progress of this case is being watched with interest.

Partial Hepatectomy and Right Hemicolectomy for Carcinoma of the Hepatic Flexure of the Colon.—RONALD W. RAVEN, O.B.E., F.R.C.S.

Male, aged 38, was admitted to the Royal Cancer Hospital with symptoms extending over one year. Two months before admission another surgeon performed an exploratory laparotomy and found a carcinoma of the hepatic flexure of the colon invading extensively the right lobe of the liver. This was considered inoperable and a palliative ileo-transverse colostomy was performed. The patient's condition was deteriorating rapidly, he was wasted and had severe secondary anæmia—R.B.C. 1,900,000 per c.mm., Hb 28 %. The patient and his wife urged that an attempt should be made to eradicate the tumour and after careful preparation, including the transfusion of large amounts of blood, operation was performed. A large part of the right lobe of the liver, including the gall-bladder and the right half of the colon, was excised. No evidence of secondary carcinoma, apart from the liver extension, was found. Patient made an excellent recovery from the operation.

(A full report of this case appeared in the *British Medical Journal*, 1947 (ii), 249.)

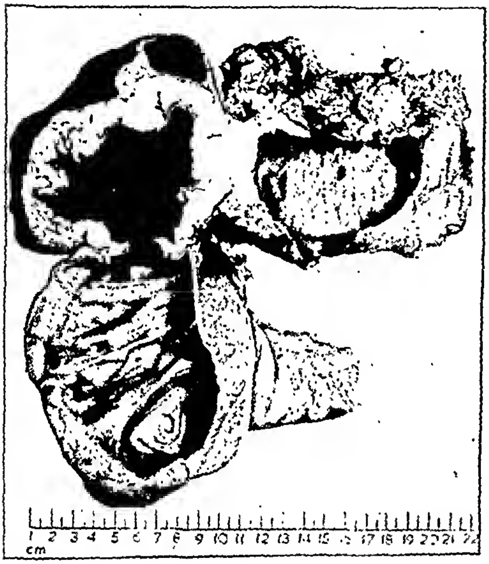


FIG. 1.

Specimen removed at operation showing a part of the right lobe of the liver, gall-bladder and right half of the colon. A large carcinoma of the hepatic flexure of the colon is invading extensively the right lobe of the liver.

[*May* 14, 1947]

DISCUSSION ON

CONGENITAL ANOMALIES OF THE ANORECTAL REGION

Professor John Kirk: *A résumé of the developmental anatomy of the rectum and anal canal.*—The portion of the embryonic gut supplied by the inferior mesenteric artery extends from the distal part of the transverse colon to the junction of the upper two-thirds with the lower third of the anal canal and is termed the "hind-gut". At an early stage it gives off a ventral diverticulum, the allantois, which, passing forwards and upwards into the umbilical stalk, carries with it the two allantoic vessels which will become the umbilical arteries of the placenta. Immediately proximal to the base of the allantois two lateral ridges form on the inner surface of the gut wall and by meeting and fusing in the mid-line form a urorectal septum. This extends caudalwards in a coronal plane and divides the gut-tube at first partially, but finally completely, into a ventral (urogenital) and a dorsal (rectal) compartment.

The genital ducts and the ureters retain their connexion with the urogenital compartment and behind it are embedded in the septum. At first both compartments are shut off from the surface by the cloacal membrane. On the external aspect of this two shallow depressions are discernible; the anterior of these represents the future urogenital cleft and the posterior one (the proctodæum) is destined to form the lower half-inch of the anal canal.

In the eighth week the membrane breaks down and the two passages open on the

In the frog both bladder and rectum open into a common cloacal outlet and the genital ducts (which in the male function both as ureters and vasa deferentia) have their separate openings into the same passage a little more distally. In the female the Wolffian ducts act solely as ureters and they, as well as the oviducts, open separately into the cloacal chamber.

In reptiles, on the other hand, while there is still a common cloacal outlet for bladder and rectum, the two passages are now partially separated by a short septum into a ventral (urogenital) and a dorsal (rectal) compartment. In the male the ureters are distinct for a short distance only and unite with the vasa deferentia before opening into the cloaca. In the female the ureters and the oviducts open into the chamber separately.

In the monotremes—those primitive oviparous mammals represented by the platypus and the echidna—the division of the cloaca, though still incomplete, is carried a stage further. The vasa deferentia of the male are now completely separated from the ureters and all four channels open on the floor of the urogenital sinus which has become elongated to form a urethra.

In the marsupial mammals yet another stage is reached. The urorectal septum is almost, but not quite, complete and the rectum and urogenital passages still communicate with each other close to the perineum. A common sphincter muscle, however, surrounds the anal and urogenital openings which lie just within the cloacal aperture.

In the higher mammals we find for the first time the formation of a perineal body with complete separation of the anal and urogenital passages.

All these successive stages can be seen taking place in the developing human embryo. In the fifth week the rectum ends as in the frog; in the sixth week the condition is similar to that found in the monotremes, and early in the seventh week the urorectal septum is complete and the perineal body is formed. At this date, however, the cloacal membrane is still intact but on its external surface two shallow depressions are discernible, the anterior one representing the future urogenital cleft and the posterior one (the proctodæum) destined to form the anal opening and lower third of the anal canal.

Early in the eighth week the membrane breaks down and the anal canal is complete. There is thus enacted a drama of progressive development presenting a transition from amphibian, reptilian, and primitive mammalian anatomy to its perfection in the human perineum. It is worth noting that at this same time in the embryological calendar the development of the human face reaches completion by the fusion of its several processes.

A study of congenital malformations of the rectum and anus in man becomes an open book to those who remember those simple but salient facts in the embryology and comparative anatomy of this region.

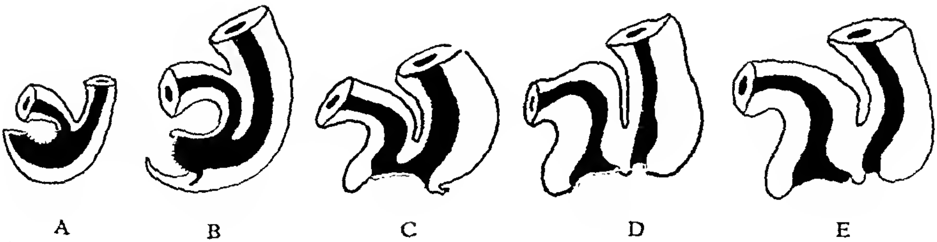


FIG. 2.—Hind-gut of human embryo: A, at four weeks; B, at five weeks; C, at six weeks; D, at seven weeks; E, at eight weeks.

REFERENCES

[1] KEITH, ARTHUR (1933) Human Embryology and Morphology. 5th Ed., Chap. 26.
[2] JONES, F. WOOD. *J. Anat.*, 1914, 48; 1915, 49; 1916, 50.

Professor R. A. Willis: *Comments on Sacrococcygeal Teratomas.*—

I. Distinction of Teratomas from other Regional Malformations

A teratoma is a true tumour containing multiple tissues foreign to the part. The presacral teratomas should be distinguished sharply from the following three kinds of malformations, with which they have been confused but to which they are unrelated:

The lower area distal to the pecten, however, is supplied by *somatic nerves* (the *inferior* hæmorrhoidal branch of the pudendal nerve and the perineal branch of the fourth sacral). Its muscle ring—the external sphincter—is striped and voluntary, and its mucous membrane is exquisitely sensitive. Its lymphatic vessels drain with the peri-anal skin to the superficial set of subinguinal glands. As far as vascular supply is concerned the same embryonic line demarcates the anastomosis of the arterial stream from the superior hæmorrhoidal artery of the pelvis with the inferior hæmorrhoidal artery of the ischiorectal fossa. It is rare to find a middle hæmorrhoidal artery of any size. If present, its origin usually shares a common stem with the inferior vesical branch of the internal iliac. The venous drainage has a corresponding arrangement and across the boundary line there is a *freely communicating* network linking the portal and systemic venous systems.

There are three spaces in relation to the rectum and anal canal which are of embryological significance and of much practical importance. The ischiorectal fossa which lies below and external to the levator ani is divided by a layer of fascia, the tegmentum ("lunate fascia" of Elliot Smith), into an infra- and a suprategmental compartment. This fascia represents the deep fascia of other regions. On the medial wall of the fossa it is attached, as is to be expected, to the upper edge of the external sphincter, i.e. at the level of the pecten, and laterally it fuses with the fascia over the obturator internus to form a sheath for the pudendal vessels (Alcock's canal). Superficial to the tegmentum is the subcutaneous fat and loose areolar tissue of the ischiorectal fossa. In the suprategmental space the fat is less in amount and the areolar tissue has a finer texture. It is limited above and medially by the perineal surface of the levator ani covered by its anal fascia. Above the levator ani and surrounding the lower one-third of the rectum is the extraperitoneal fat and connective tissue which covers the pelvic floor. Into this perirectal space an ischiorectal abscess *may, under certain circumstances,* extend.

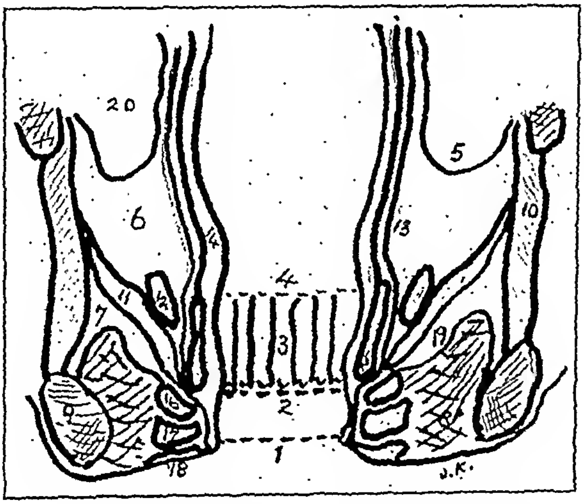


FIG. 1.—Coronal section of pelvis (diagrammatic): 1, Anal orifice. 2, Pectinate line and anal valves (formerly site of attachment of cloacal membrane). 3, Anal columns. 4, Anorectal junction. 5, Peritoneum. 6, Perirectal space. 7, Supracegmental space. 8, Infrategmental space. 9, Ischial tuberosity. 10, Obturator internus. 11, Iliococcygeus. 12, Pubococcygeus and puborectalis (anorectal sling). 13, Longitudinal muscle of rectum. 14, Circular muscle of rectum. 15, Internal sphincter. 16, 17, 18, Deep, superficial and subcutaneous parts, respectively, of external sphincter. 19, Tegmentum (deep fascia of ischiorectal fossa). 20, Peritoneal cavity.

THE VALUE OF COMPARATIVE ANATOMY

The comparative anatomy of this region is as illuminating as its embryology and we owe much to Sir Arthur Keith [1] and Professor Wood Jones [2] for their elucidation of this subject.

In the frog both bladder and rectum open into a common cloacal outlet and the genital ducts (which in the male function both as ureters and vasa deferentia) have their separate openings into the same passage a little more distally. In the female the Wolffian ducts act solely as ureters and they, as well as the oviducts, open separately into the cloacal chamber.

In reptiles, on the other hand, while there is still a common cloacal outlet for bladder and rectum, the two passages are now partially separated by a short septum into a ventral (urogenital) and a dorsal (rectal) compartment. In the male the ureters are distinct for a short distance only and unite with the vasa deferentia before opening into the cloaca. In the female the ureters and the oviducts open into the chamber separately.

In the monotremes—those primitive oviparous mammals represented by the platypus and the echidna—the division of the cloaca, though still incomplete, is carried a stage further. The vasa deferentia of the male are now completely separated from the ureters and all four channels open on the floor of the urogenital sinus which has become elongated to form a urethra.

In the marsupial mammals yet another stage is reached. The urorectal septum is almost, but not quite, complete and the rectum and urogenital passages still communicate with each other close to the perineum. A common sphincter muscle, however, surrounds the anal and urogenital openings which lie just within the cloacal aperture.

In the higher mammals we find for the first time the formation of a perineal body with complete separation of the anal and urogenital passages.

All these successive stages can be seen taking place in the developing human embryo. In the fifth week the rectum ends as in the frog; in the sixth week the condition is similar to that found in the monotremes, and early in the seventh week the urorectal septum is complete and the perineal body is formed. At this date, however, the cloacal membrane is still intact but on its external surface two shallow depressions are discernible, the anterior one representing the future urogenital cleft and the posterior one (the proctodæum) destined to form the anal opening and lower third of the anal canal.

Early in the eighth week the membrane breaks down and the anal canal is complete. There is thus enacted a drama of progressive development presenting a transition from amphibian, reptilian, and primitive mammalian anatomy to its perfection in the human perineum. It is worth noting that at this same time in the embryological calendar the development of the human face reaches completion by the fusion of its several processes.

A study of congenital malformations of the rectum and anus in man becomes an open book to those who remember those simple but salient facts in the embryology and comparative anatomy of this region.

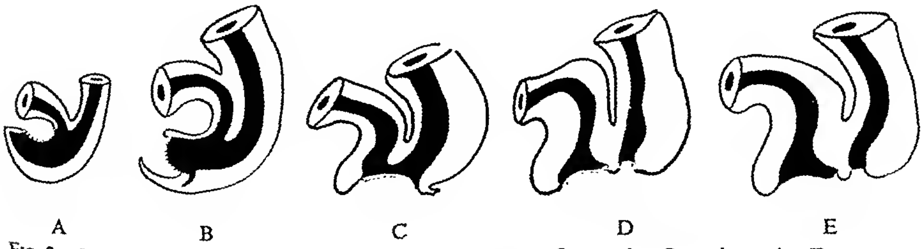


FIG. 2.—Hind-gut of human embryo: A, at four weeks; B, at five weeks; C, at six weeks; D, at seven weeks; E, at eight weeks.

REFERENCES

[1] KEITH, ARTHUR (1933) Human Embryology and Morphology. 5th Ed., Chap. 26.
[2] JONES, F. WOOD. *J. Anat.*, 1914, 48; 1915, 49; 1916, 50.

Professor R. A. Willis: *Comments on Sacrococcygeal Teratomas.*—

I. Distinction of Teratomas from other Regional Malformations

A teratoma is a true tumour containing multiple tissues foreign to the part. The presacral teratomas should be distinguished sharply from the following three kinds of malformations, with which they have been confused but to which they are unrelated:

(*a*) *Caudally attached twins:* Reconstructional studies show that teratomas never contain a vertebral axis nor show orderly regional distribution of parts.

(*b*) *Supernumerary limbs:* These are always externally attached and they contain only limb structures. Teratomas sometimes contain well-developed digits and perhaps other parts of limbs, but these are internal ingredients of the teratoma itself and are always accompanied by other kinds of tissues.

(*c*) *Residues of post-anal gut or neural canal:* The suggestion of Meyer and others that teratomas arise from such residues can be rejected; this is purely speculative, ignores the obvious fact that the presacral teratomas are essentially similar to the retroperitoneal teratomas in general, and of course fails to account for the many other tissues which they contain.

II. Structure of Presacral Teratomas

Skin, respiratory and alimentary epithelium, choroid plexus, neuroglial tissue, nerves and nerve ganglia, pancreatic or gastric tissue, skeletal and smooth muscle, bone and cartilage are all common components. Highly organized structures, such as digits or coils of intestine, are not unusual; they have often misled pathologists into interpreting teratomas as reduced fœtuses. Malignancy in sacral teratomas often involves papillary glandular components, possibly of the nature of choroid plexus; and malignant change may occur at an early age, even in infancy.

III. The Nature of Teratomas

Structural studies alone suffice to disprove the still prevalent view that teratomas represent included fœtuses. Their explanation is to be sought rather in disturbances of the chemistry of early embryonic growth, disturbances resulting in partial isolation or release of foci of embryonic tissue from the action of the primary organizer, and at the same time their neoplastic conversion. The early age at which teratomas are present—especially obvious with the presacral group—and their distribution in parts of the body derived from median or paramedian prevertebral structures, accord with this concept.

Section of Surgery

President—ERNEST FINCH, M.D., M.S., F.R.C.S.

[April 2, 1947]

Technique and Value of Tattooing in Plastic Surgery

By D. N. MATTHEWS, O.B.E., M.Ch., F.R.C.S.

TATTOOING is a very ancient art. It has been practised through all ages all over the world. Primitive tribes used thorns with tree-gum soot as the tattooing medium, whilst Egyptian craftsmen designed fine gold rakes and gold hammers with which to drive in an infinite variety of coloured pigments. The modern apparatus consists of a needle connected to a vibrator electrically driven.

Dangers.—In the past infection was a common sequel to tattooing and not infrequently caused death. Transmission of syphilis occurred so often that tattooing was declared illegal by the Army authorities of many nations. But with strict adherence to modern aseptic technique, these risks are completely eliminated. The possible toxicity of the dyes is the only danger to-day, and it is wise to make several small test tattoos of any new dye before accepting it into general use.

Dyes.—These must be relatively insoluble, stable to light and unaffected by tissue reaction. The reaction they excite must be slight and only transient and they must have no toxic systemic action. I have used ochres, which are oxides of iron, in shades of brown and red supplied to me by Imperial Chemical Industries. I have also used cadmium selenides, supplied by the Blythe Colour Works, in nine shades ranging from tangerine, through yellow and pink to brick red. I have not used mercuric sulphide (cinnabar) since it can cause severe mercurial poisoning, although it has been recommended by tattooists for cosmetic purposes and is used by dermatologists in the treatment of pruritus. I.C.I. and the Blythe Colour Works naturally disclaimed all responsibility for any toxic or other untoward effect the injection of these pigments might produce, but gave me all possible assistance.

Tattooing instrument.—My tattooing machine is an adaptation of one I bought from a professional. It consists of a simple electric "make and break" vibrator working against a small spring load with a 3 mm. travel. A four-volt battery or rheostat control from the electric light drives it. The head of the vibrator contains nine needles set close and arranged to give an even track of punctures (fig. 1).

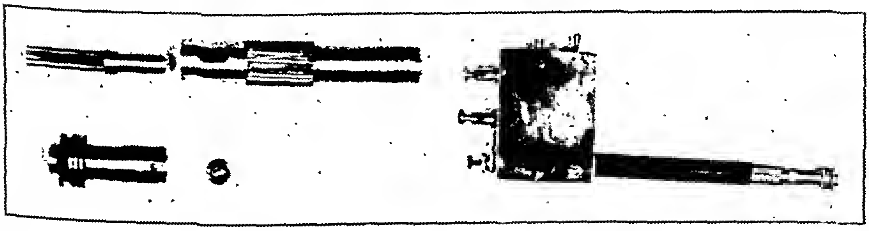


FIG. 1.—Tattooing machine (designed by author) with detachable head, containing nine needles. Driven by 4 volt current.

Technique.—Authentic medical literature is scanty and in the few articles published the technique recommended is to obtain the requisite shade by mixing the dyes with a white base. Zinc oxide and barium sulphate have both been advocated for the purpose. But in my experience such mixtures always give an ugly, blotchy appearance when tattooed, despite an excellent colour match *in vitro*. This was so whether the powders were mixed dry or with alcohol. It seemed that the only way to get a good result was to possess a large enough variety of shades for all requirements, (*a*) *Caudally attached twins*: Reconstructional studies show that teratomas never contain a vertebral axis nor show orderly regional distribution of parts.

(*b*) *Supernumerary limbs*: These are always externally attached and they contain only limb structures. Teratomas sometimes contain well-developed digits and perhaps other parts of limbs, but these are internal ingredients of the teratoma itself and are always accompanied by other kinds of tissues.

(*c*) *Residues of post-anal gut or neural canal*: The suggestion of Meyer and others that teratomas arise from such residues can be rejected; this is purely speculative, ignores the obvious fact that the presacral teratomas are essentially similar to the retroperitoneal teratomas in general, and of course fails to account for the many other tissues which they contain.

II. Structure of Presacral Teratomas

Skin, respiratory and alimentary epithelium, choroid plexus, neuroglial tissue, nerves and nerve ganglia, pancreatic or gastric tissue, skeletal and smooth muscle, bone and cartilage are all common components. Highly organized structures, such as digits or coils of intestine, are not unusual; they have often misled pathologists into interpreting teratomas as reduced fœtuses. Malignancy in sacral teratomas often involves papillary glandular components, possibly of the nature of choroid plexus; and malignant change may occur at an early age, even in infancy.

III. The Nature of Teratomas

Structural studies alone suffice to disprove the still prevalent view that teratomas represent included fœtuses. Their explanation is to be sought rather in disturbances of the chemistry of early embryonic growth, disturbances resulting in partial isolation or release of foci of embryonic tissue from the action of the primary organizer, and at the same time their neoplastic conversion. The early age at which teratomas are present—especially obvious with the presacral group—and their distribution in parts of the body derived from median or paramedian prevertebral structures, accord with this concept.

reverse of any published recommendations I have been able to find. If placed superficially as has been advocated, the scarred epithelium blisters and the dye is lost.

Finally two patients were tattooed with a light shade of pink in an attempt to hide the pigmentation left by burns. These were failures as the pigment was so superficially placed that it was impossible to cover it. The dye always went too deep.

Mr. D. C. Bodenham: What is the best particle size to select in powders used for tattooing: and has Mr. Matthews any further information on the tattooing of dark areas with light colours?

Mr. D. N. Matthews (in reply): The smaller the particle size the better. I am at present trying to replace the pigmented areas with white, using zinc oxide and then colouring the white base as required. It is too early to say whether this is going to prove satisfactory. Technically it is difficult.

[*May* 3, 1947]

MEETING HELD AT THE ROYAL HOSPITAL, SHEFFIELD

Some Dermatological Complications of Open Wounds

By I. B. SNEDDON, M.B., Ch.B., M.R.C.P.

THE dermatitis which may complicate open wounds, and by that I mean any granulating surface whatever the cause, is an important type, not from the numbers of cases which occur, but because many of the cases may be prevented. It is often affirmed that dermatitis cannot be cured and there is an element of truth in this. So many of our chronics could have got through life without trouble if it had not been for a precipitating cause, therefore any method of prevention is valuable.

If dermatitis does occur it may prolong unduly the treatment of a simple surgical case by delaying later surgical procedures. Dermatitis after amputations may make an otherwise satisfactory stump useless. The pathology of dermatitis consists essentially of the formation of vesicles in the epidermis by a combination of extracellular œdema and destruction of the cells by intracellular œdema. The vesicles rupture, leaving a moist, weeping surface which later becomes crusted.

The types of dermatitis which may affect the skin surrounding a granulating surface may be classified as:

(1) Traumatic.
(2) Sensitization. — (*a*) Chemical.
(*b*) Bacterial.

(1) *Traumatic dermatitis.*—This is caused by the direct physico-chemical action of agents, such as acids and alkalis, and the stronger antiseptics, such as iodine and picric acid. The mechanism of this type of eruption is obvious and its prevention simple.

(2) *Sensitization dermatitis.* (*a*) *Chemical.*—To produce this the chemical agent has to act for some time on epithelial cells which eventually become sensitized. At this stage further contact with the agent causes dermatitis. The classical experiments of Cranston Low, who made a group of individuals sensitive to primula leaves, illustrate this mechanism. Bloch showed that idiosyncrasy was only a matter of degree and that everyone could be sensitized if concentration and time of application were increased. Granulating surfaces are particularly prone to become sensitized as the epithelial cells are exposed to closer contact with external agents than in intact skin. The site of a wound is also important. Where the blood supply is poor the epidermis is more prone to sensitization, owing to the longer time of healing and also the poorer nutrition of the cells.

Of the popular applications which may give rise to dermatitis the following are of topical interest:

(i) *Acridines.*—Acriflavine is a common cause of dermatitis, much more common than the literature would suggest. During the last ten years only two cases have been published, by Beare (1947) and Young and Hawking (1938). Acriflavine also has the effect of lighting up sulphonamide dermatitis and Russell and Beck (1944) showed that proflavine and sulphonamide mixtures were more lethal to tissues than either substance singly.

and to tattoo each separately where it was needed. This method has proved satisfactory. The colour of normal skin consists of brown and pink in varying proportions and shades with the superadded stubble of the hirsute areas in men.

My practice has been to tattoo the brown colour first, matching the amounts and shades to the opposite side of the face if present. A little overlapping softens the change from one colour to another provided a considerable reduction is made in the quantity of both dyes used in the overlap; otherwise the overlap is too dark.

Areas can be marked off in Bonney's blue and tattooed, and the spaces between them blended by overlapping. Owing to a diffusion of the points of colour, they become more apparent after a few weeks. All areas should therefore be slightly undercoloured especially when beard and moustache stubble are being tattooed. This diffusion is probably due to entry of the dye into the tracks of the hair follicles and sweat ducts. An interval of one month should be made between brown and pink tattooing and again before hair stubble is added. For this, dark brown dye is more satisfactory than black as the latter looks dirty.

The procedure is carried out with full aseptic theatre routine and sterilization of the skin and detachable parts of the vibrator. The dyes are not autoclaved owing to colour changes which heat would produce. They are, however, mixed with absolute alcohol. The paste which results is painted on the surface to be tattooed and the instrument pressed into it with the needles vibrating and held at right angles to the skin. Insertion of the dye is facilitated if the skin is stretched slightly. In unsupported regions such as the cheek, a finger must be inserted into the mouth for counterpressure. The dye should be driven into the dermis and the basal layer of the epidermis. Insertion at this level causes minute pin-point hæmorrhages which are useful guides to the correct level. If it is put in the superficial layers of the epidermis there is no bleeding. Most of the dye inserted at this level is rubbed away within a few months. It is probably true that a little of the dye inserted in the dermis is ultimately deposited in the lymphatics. To avoid disfiguring lines or blurred marks, the collar of the vibrator must be so adjusted that the needles disappear behind it with each vibration; this allows a 2 to 3 mm. travel. The instrument must be moved very slowly over the skin for the same reason; no more than 1 cm. of movement should be made in one minute. It is impossible to drive dry powder into the skin, and as the alcohol evaporates rapidly it is convenient to cover only about half a square inch with the paste at a time. When each area has been traversed the excess dye is washed away with ether to assess how much has been driven in. I have not found an anæsthetic to be necessary. The pricking sensation is only uncomfortable initially. Injections of local anæsthetic prevent accurate judgment of depth. The tattooed area is covered with tulle gras, backed with sterile gauze and smeared with penicillin cream. Irritation and slight œdema sometimes occur, but disappear in forty-eight hours. The dressing is discarded a day or two later.

Uses and results.—Tattooing is a valuable adjunct to the plastic repair of facial wounds and burns. The colour match of free grafts and pedicle flaps in such cases is often poor and can be considerably improved. In addition a hirsute appearance can be given to the beard area, a missing eyebrow can be simulated and the vermilion border added to a flap replacing a lost lip. I have tattooed 21 patients. Fifteen required tinting of free grafts and flaps, and beard stubbling; this group gave the most satisfactory results. A very fair degree of normality can be restored and for them tattooing finds its greatest usefulness.

Two patients required eyebrow disguise; these were reasonably satisfactory but could have been better if tattooing had been done in lines rather than dots. This could have been effected by adjusting the needles so that they did not quite disappear behind the collar of the vibrator with each vibration. Two patients had scars left by X-rays, and were more successful than I had expected. Scar tissue is difficult to tattoo and it is necessary to drive the dye deeper than for normal skin. This is the

Section of Orthopædics

President—V. H. ELLIS, F.R.C.S.

[*March* 4, 1947]

THE following cases were shown:—

Abnormal Ossification in Scapular Region.—Mr. DAVID TREVOR.

(1) Chronic Osteomyelitis: Multiple Foci Including Spine; (2) Gross Shortening of Leg and Deformity of Knee Associated with Tuberculous Disease of the Hip.—Mr. J. A. CHOLMELEY.

(1) Excision Head and Neck of Femur and Sub-trochanteric Osteotomy for Unilateral Osteo-arthritis of the Hip: Female, Aged 40; (2) Excision Head and Neck of Femur and Sub-trochanteric Osteotomy for Irreducible Fracture Dislocation of the Hip: Two Males, Aged 20 and 22 respectively; (3) Excision Head and Neck of Femur and Sub-trochanteric Osteotomy for Pyogenic Arthritis of the Hip: Child, Aged 9; (4) X-ray Films of Two Cases Showing an Unusual Form of Osteochondritis of the Patella in Adolescent Males.—Mr. J. S. BATCHELOR.

[*May* 6, 1947]

Recurrent Dislocation of the Elbow-Joint

By D. WAINWRIGHT, F.R.C.S.Ed.

RECURRENT dislocation occurs most commonly at the shoulder-joint but the condition does occasionally arise at the other joints, e.g. the temporomandibular joint, the sterno-clavicular joint, and the carpo-metacarpal joint of the thumb, and as a subluxation at the ankle-joint.

In the literature I have only been able to find a description of three previous cases of recurrent dislocation of the elbow-joint. The first case was described by Sorrel in 1935; in 1936 Henry Milch reported a case of bilateral recurrent dislocation and in 1943 Gosman of Wisconsin reported a unilateral case.

The following is an illustrative case:

Albert T., aged 12, was referred to the Orthopædic Hospital, Stoke-on-Trent, on 3.12.45. He first dislocated the right elbow-joint as a result of a fall when he was 10. The dislocation was reduced and the elbow immobilized in flexion with a collar-and-cuff sling for two weeks. The dislocation recurred on five subsequent occasions, each time as a result of a trivial injury—usually with the joint in a position of almost full extension—and on each occasion the dislocation was reduced under gas and oxygen anæsthesia. On the fifth occasion the elbow was immobilized in plaster for eight weeks.

The only abnormality seen on examination of the elbow at any time was a slight degree of hyperextension of the joint when compared with the normal side, and the X-ray suggested a rather shallow olecranon fossa with a little deficiency in the depth of the coronoid process.

It was decided to provide an anterior bone block by inserting a flat bone graft into the coronoid process, and on 5.12.45 this was carried out. Under anæsthesia it was possible to reproduce the dislocation by a combination of downward traction and backward thrust of the forearm.

Under a tourniquet the anterior aspect of the joint was exposed by exploring the sulcus between biceps and the brachioradialis and splitting the fibres of the brachialis anticus protecting the musculospiral nerve. The anterior part of the capsule of the joint was found to be lax and an incision was made through it over the coronoid process and, using a small osteotome, a groove was prepared in the process for reception of the graft.

(ii) *Sulphonamides.*—The danger of sulphonamide dermatitis in this country has been exaggerated, but it is so distressing that it must be avoided at all costs.

Sulphonamides taken internally are free from the danger of causing dermatitis although they may cause toxic morbilliform eruptions. Apart from the usual type of contact dermatitis caused by sulphonamides they may produce sensitivity to sunlight. For this no cure has been found as desensitization to sulphonamide does not relieve it. It is difficult to assess the incidence of sulphonamide dermatitis but Peterkin (1945), in a review of the literature, quoted that of 1,052 cases treated by sulphonamides 35 developed dermatitis.

(iii) *Penicillin.*—The local use of penicillin is remarkably safe. Michie and Baillie (1945) report only one case of penicillin sensitivity to powder in 30,000 casualties in the British Liberation Army. Vickers (1946) and Bedford (1946) also report cases.

The remaining reports in the literature are all of doctors and technicians handling penicillin in high concentration for long periods.

It certainly seems that it takes thirty to forty days for penicillin sensitivity to develop and that powder is more dangerous than cream or solution.

There is, however, a phenomenon of aggravation of the wound without definite dermatitis. It is impossible to demonstrate penicillin sensitivity by patch tests in these cases, and it appears to be a purely local sensitivity which disappears when penicillin therapy is stopped. Wright and Gross (1947) have also found no explanation for this phenomenon.

(*b*) *Bacterial sensitization.*—The skin surrounding a wound may become sensitized to the bacteria or their breakdown products. It is commonly seen around traumatic ulcers of the leg or when a purulent wound is encased in plaster of Paris. A later phenomenon is a generalized vesicular eruption on the remainder of the body after an area of dermatitis has been aggravated or encased in an occlusive dressing. This autosensitization was described by Whitfield in 1930. Recent work by Hecht *et al.* (1943) has suggested that autosensitization is due to blood-stream spread of broken-down skin proteins, combined with local staphylococcal infection.

Prevention

As a dermatologist I would say: (1) Never put anything on the skin unless it is absolutely essential. Local treatment should be limited to dry dressings, saline, tulle gras and possibly penicillin cream. Sulphonamides should not be used. (2) Pre-operative preparation of the skin should be reduced to washing with soap and water and removal of dirt by cetavlon. Iodine and biniodide should not be used. (3) If there is already a pyogenic infection of the skin it should not be enclosed in plaster of Paris. (4) Chemotherapy should be given parenterally or by mouth.

In support of this I would like to quote the conclusions of an American surgeon, Dr. C. Lyons (1947), reviewing the treatment of war wounds, who states that local chemotherapy is unnecessary and undesirable.

BIBLIOGRAPHY

Beare, J. M. (1947) *Lancet* (i), 410.
Bedford, P. D. (1946) *Brit. med. J.* (i), 51.
Bloch, B. (1928) *Klin. Wschr.*, 7, 1065.
Hecht, Rudolph, Sulzberger and Weil (1943) *J. exp. Med.*, 78, 59.
Low, Cranston (1924) Anaphylaxis and Sensitization. Edinburgh.
Lyons, C. (1947) *J. Amer. med. Ass.*, 133, 215.
Michie, W., and Bailie, H. W. C. (1945) *Brit. med. J.* (i), 554.
Peterkin, G. (1945) *Brit. med. J.* (ii), 1.
Russell, D. S., and Beck, D. J. K. (1944) *Brit. med. J.* (i), 112.
Vickers, H. R. (1946) *Lancet* (i), 307.
Whitfield, A. (1930) Autosensitization Eczema, *Int. derm. Congr.*, Copenhagen, 142.
Wright, C. S., and Gross, E. R. (1947) *Arch. Derm. Syph.*, 55, 52.
Young, W. A., Hawking, F. (1938) *Lancet* (i), 1275.

A paper on Treatment of Cerebral Abscess was read by Mr. James Hardman. This was based on work carried out with Professor Wilson Smith, in preparation for a joint paper.

(1) *Waldenström's Sign and the Ligamentum Teres*

Waldenström (1938) of Stockholm, described as an early sign an increased distance between the medial pole of the head and the floor of the socket. We have found Waldenström's sign very frequently and not uncommonly on the first film that showed changes in opacity. It is not very marked in the earliest stage but becomes more so in the following months if the hip is not put to rest. Then it may reach such a degree that the shadows of the femoral head and the ischial bone no longer overlap but leave a gap between them (fig. 1). Waldenström believes that his phenomenon is due to an effusion into the joint. We cannot agree with him for several reasons. The effusion found at operations was always negligible in amount and never under sufficient tension to distend the capsule, let alone displace the femoral head. An effusion under high tension would cause severe clinical symptoms. It would push the head downward as well as outward. Finally, the arthrogram would show marked pooling of contrast medium in the space in question.

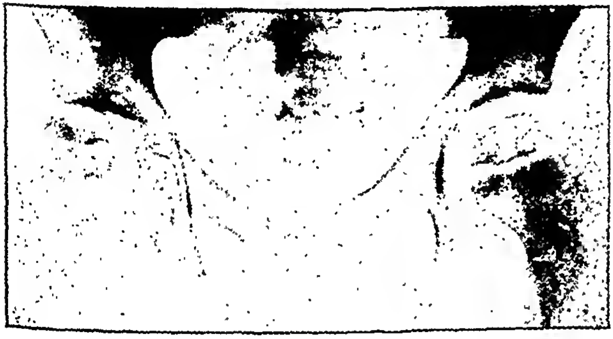


FIG. 1.

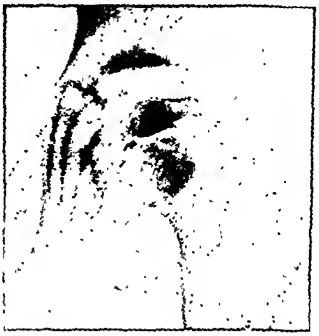


FIG. 2.

FIG. 1.—Untreated case. The shadows of femur and ischium do not overlap. Excavation of acetabular floor.

FIG. 2.—Arthrogram. No pooling of contrast medium in socket. In the lower part of the latter there are two thin deposits separated by soft parts.

The arthrogram (fig. 2) was taken before a perfect technique had been evolved but it shows clearly that there is no pooling between head and socket. There is, however, medial to the head contour, another narrow space filled with contrast medium, but between this and the surface of the head there is a translucent area. This area can only contain some soft structure. Closer scrutiny of the previous X-ray (fig. 1) reveals a feature that sheds more light on the problem. The acetabular floor is altered. It does not show the same rounded contour, continuing that of the roof, as on the other side but is hollowed out abruptly. This excavation of the acetabular floor becomes apparent very much later than Waldenström's sign but is never seen in the latter's absence. Both signs can be observed occasionally in hips with inflammatory lesions, such as tubercle.

A picture like this suggests that there is something between the bony parts, pressing the femoral head outward and the floor of the socket inward. In this situation lie the Haversian pad of fat and the round ligament. Whitman (1929), when he opened a hip-joint in a case of pseudocoxalgia, found the ligamentum teres grossly swollen and congested, and a similar observation was made in a case of the present series. The inference seems justified that it is the congested, hyperæmic, throbbing ligamentum teres that causes both Waldenström's sign and the excavation of the acetabular floor, much as an aortic aneurysm displaces the viscera and erodes the spine.

Both Milch and Gosman used a *tibial graft*; but there appeared to be no point in looking elsewhere for bone, and a flat cortical graft about ¾ in. × ½ in., and about ¼ in. thick, was taken from the subcutaneous portion of the upper end of the ulna and forced firmly into the groove. The anterior capsule was closed and reefed longitudinally, the wound closed, and the elbow immobilized in plaster at a right angle for two months.

The series of X-rays [demonstrated at the meeting] show very clearly the degree of absorption of the graft, the substitution of new bone and the process of remodelling and moulding which has taken place and which has occurred much more rapidly than one would have expected.

In spite of the prolonged immobilization, movements returned fairly rapidly and radiographically, at any rate, the bone block appears to be adequate to prevent further dislocation.

Pathology.—The underlying pathology of this condition appears to differ in the cases which have been described.

Sorrel's case was associated with a marked relaxation of the ulnar collateral ligament and in his case the dislocation was associated with an outward gliding movement of the ulna.

In the case described by Milch (which was bilateral) there appears to have been a true congenital abnormality of the greater sigmoid cavity, which was very shallow.

Gosman's case, on the other hand, showed no radiological abnormality but was associated with hypermobility of the joint and general laxity of the ligaments.

In the case just described, I think the main factor was the deficiency in depth of the coronoid process: when the joint was exposed at operation this process appeared to have a smooth, rounded beak, providing a very inefficient check to forward displacement of the lower end of the humerus. There was, in addition, some general laxity of the capsular ligaments, but this was felt to be rather a secondary result of the repeated dislocations.

Treatment.—So far as treatment is concerned there appeared to be three possible ways of tackling the problem: Reefing the collateral ligaments might have been tried but, on the whole, capsuloplasties are not very successful; or the convexity of the sigmoid notch could be modified by an osteotomy of the coronoid process.

The soundest procedure, however, appeared to be some type of bone block. An osteotomy and forward flexion of the tip of the olecranon process, to prevent full extension of the elbow, might have succeeded; but an anterior bone block appeared to be more rational. This was the method used successfully by both Milch and Gosman. Milch employed a curved, boomerang-shaped, cortical graft from the tibia to form a continuous line with the curve of the coronoid process. A rectangular graft is much simpler to cut and insert, and subsequent X-rays demonstrate clearly the remodelling which occurs during the process of absorption and substitution of new bone.

Pseudocoxalgia: (Calvé-Legg-Perthes' Disease)

The Radiographic Changes Outside the Femoral Head

By H. G. KORVIN, F.R.C.S.

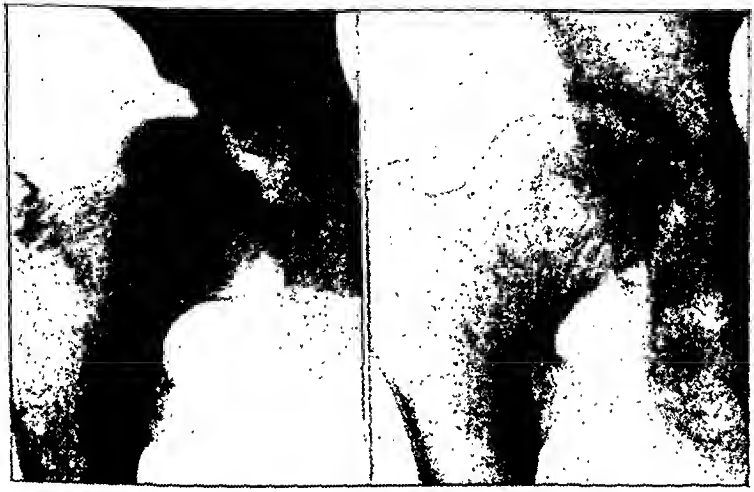
In a previous paper (Korvin, 1947) the radiographic changes in the femoral epiphysis seen in pseudocoxalgia have been discussed. The conclusion arrived at was that they conform to the pattern of ischæmic necrosis and that it is unnecessary to assume a pathological lesion not met with elsewhere in the body. The changes outside the epiphysis have generally been given less attention, but have occasionally been described as an extension of the disease process from the femoral head into the neck and acetabulum. In the following an attempt will be made to interpret these, too, in terms of recognized pathology. The conclusions are based on the study of 90 cases with 102 affected hips, seen at Biddulph Grange Orthopædic Hospital (54), Ethel Headley Hospital (26), and Manchester Royal Infirmary (10).[1]

---

[1] My thanks are due to Professor Platt and to Dr. Jean Bucknell.

definite zone of sclerosis. The acetabular roof shows three distinct areas, each the size of a pea, which are more translucent than the rest and, again, partly surrounded by a faint line of sclerosis. The anterior margin of the roof is made up of several rounded prominences protruding downward. They are more marked than normally besides being better visible because the bony epiphysis, reduced to a flat disc, no longer obscures them. Six years later not the slightest trace of the cyst-like appearance is visible.

In a boy aged 13 (fig. 5) the X-ray film showed a late stage of pseudocoxalgia. The outer half and the inner edge of the epiphysis are regenerated. To the inner side of the centre there is still a considerable defect. The edge of the acetabular roof shows a complete defect, nearly half an inch in diameter. The site of that defect corresponds to the attachment of the joint capsule, a structure known to be markedly congested in such cases. In the ischial part of the socket there is a less marked, round, very regular translucent area: an enlarged vascular foramen. Two years later, when the head was re-formed, the defect in the head of the acetabulum had disappeared except for a tiny notch. But the socket as a whole has become very much flattened during the time when it was deprived of much of its bony structure.



A. B.

FIG. 5.—Boy aged 13. A. Large defect at edge of acetabular roof. B. Two years later defect almost obliterated.

(3) *Deformity of the Femoral Neck*

The amount of deformation the necrotic femoral epiphysis undergoes before it regenerates is the main factor determining the ultimate shape of the upper end of the femur, but it is not the only factor. Often gross flattening of the epiphysis is associated with marked deformity of the femoral neck, resulting in coxa vara, anteversion, or retroversion.

A boy had been treated for pseudocoxalgia from his sixth to his eighth year. An anteroposterior radiograph taken at the age of 15 (fig. 6) shows, apart from marked flattening of the epiphysis, severe coxa vara deformity. The lateral view shows the anterior contour of the neck only slightly concave but the posterior contour almost semicircular, the metaphyseal end forming here an overhanging

There are, on the other hand, cases in which the arthrogram does show pooling of contrast medium between head and socket. A boy aged 6 had complained of pain in his left hip for three months. Three years earlier a congenital dislocation of his right hip had been reduced. The X-ray film showed the left femoral epiphysis flattened and denser than the rest of the bone, beginning absorption at its inner extremity, and an increased distance between the head and the acetabular floor. The roof of the socket was slightly but definitely sloping upward and outward. The arthrogram (fig. 3) reveals a considerable pool of contrast medium between femoral head and acetabular floor. In the right hip a similar pooling of contrast medium and marked sloping of the roof of the very shallow socket can be seen.

In this case there had been, associated with the dislocation of the right hip, subluxation or "dysplasia" on the left side. This is demonstrable as a sloping roof on X-ray films taken before the hip developed pseudocoxalgia. Owing to the subluxation there is room in the socket for contrast medium to collect. This, however, is an exceptional finding that can be fully accounted for. It thus confirms the rule that Waldenström's sign is not due to joint effusion.

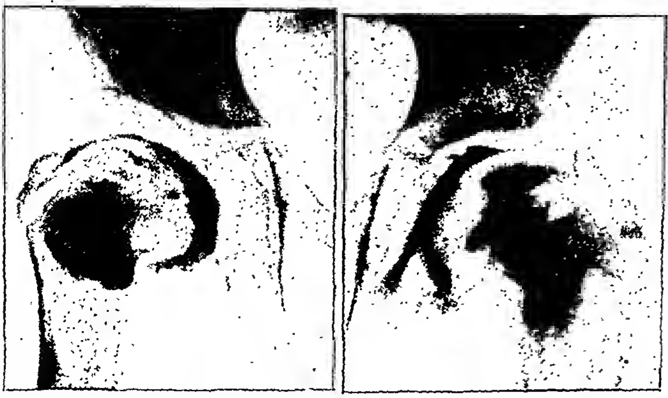


FIG. 3.—Reduced dislocation of right hip, pseudocoxalgia on left side. Both roofs sloping. Arthrograms. Pooling of contrast medium between head and socket on both sides.

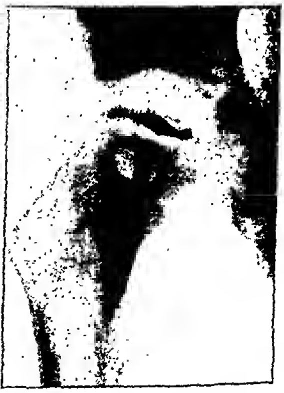


FIG. 4.—"Cyst-like spaces" in centre of neck.

(2) *Structural Changes in the Neck and Socket*

The osteoporosis of the neck and the socket observed in the early stages is diffuse and homogeneous. In severe cases the absorption of bone becomes at a later stage more complete in some parts than in others, resulting in formation of what are often termed "cystlike spaces" and, at the edge of the bone, actual defects. These areas of absorption have been wrongly described as necroses or as an extension of that undefined process "osteochondritis" into the neck and acetabulum.

Wherever osteoporosis attains a high degree and is present for long periods, such "cystlike" spaces are found. They are met with in osteo-arthritis, rheumatoid arthritis, osteomalacia, occasionally in Paget's disease, and, most characteristically, in parathyroid disease. Where the underlying condition can be cured the "cysts" can disappear again. They disappear in pseudocoxalgia by the time the epiphysis has regained its normal texture. But any deformity the skeletal parts have acquired during and on account of this extreme bone atrophy remains permanent.

In a boy aged 4 (fig. 4) the radiograph shows severe crushing of the epiphysis. Near the centre of the neck there are two cyst-like areas, partly surrounded by a on the other side. This is due to the head having another lower border which is convex and overlaps the neck. If this line is taken as the contour the epiphysis must be described as ovoid, not crescentic. In reality it is neither. It is merely tilted and therefore not seen strictly in profile, similar to the slipped epiphysis in coxa vara. It differs from the latter in that the displacement has occurred within the substance of the neck and not at the epiphyseal line. A certain degree of coxa vara is present: on the left side a line drawn through the tip of the trochanter at right angles to the shaft bisects the epiphyseal line, while on the right it lies wholly above it.

Three months later the boy developed clinical pseudocoxalgia. A radiograph taken one year after the first shows typical changes (fig. 8A). The epiphysis is relatively dense. Its outer edge is eroded. The twofold lower contour is very conspicuous: the tilting has increased. The tip of the trochanter is now level with the summit of the head. In order to determine whether the neck had bent forward or backward, films were taken with the X-rays traversing the hip obliquely. When the angle of incidence was made 30 degrees by flexing the hip by that amount the epiphysis was seen in profile and the epiphyseal line was narrow, straight, and clear (fig. 8B). The femoral neck was, therefore, bent forward.

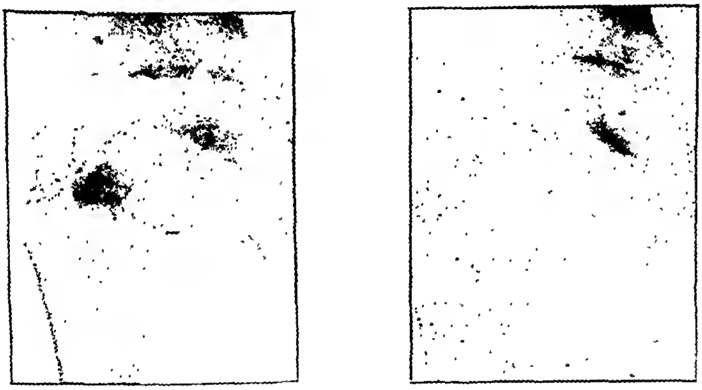

A. B.

Fig. 8.—Same case, one year later. A. Definite pseudocoxalgia. Tilting more marked. B. Normal relationships restored by flexing hip through 30 degrees.

This tilting of the epiphysis caused by forward bending of the neck is more obvious before any real deformity of the epiphysis itself has developed, i.e. in early cases. They constitute Legg's mushroom type, with its favourable prognosis. But the deformity of the neck is not an essential feature at this stage. It was seen in one-half of the early cases only. Although the demonstrable osteoporosis is not conspicuous it is the only factor that can be made responsible for the bending of the neck.

There remain to be discussed the changes in the articular cartilage. This is commonly regarded to be unaffected, as evidenced by the preservation of the radiographic joint space. Only many years later osteo-arthritis supervenes owing to incongruity of the articular surfaces in all but the very early treated cases. Very rarely—in 5% of the cases under review—the cartilage is lost early.

REFERENCES

Korvin, H. G. (1947) Spring Meeting British Orthopædic Association.
Waldenström, H. (1938) *J. Bone Jt. Surg.*, 20, 559.
Whitman, R. (1929) *Amer. J. Surg.*, 6, 791.

ledge. The epiphyseal line, just beginning to obliterate, is not set at right angles to the axis of the neck but tilted backward.

Deformity of the femoral neck can develop very early in the course of the disease, even before the head has become deformed. A boy of 8 was X-rayed because his twin brother suffered from pseudocoxalgia although he himself presented no symptoms. The radiograph (fig. 7) shows on the right side an epiphysis hardly flatter than that on the left and of equal translucency, but somewhat crescentic in shape, its lower border being, on the whole, a little concave. The adjacent part of the neck shows very slight irregular rarefaction. The epiphyseal line is not as clear as

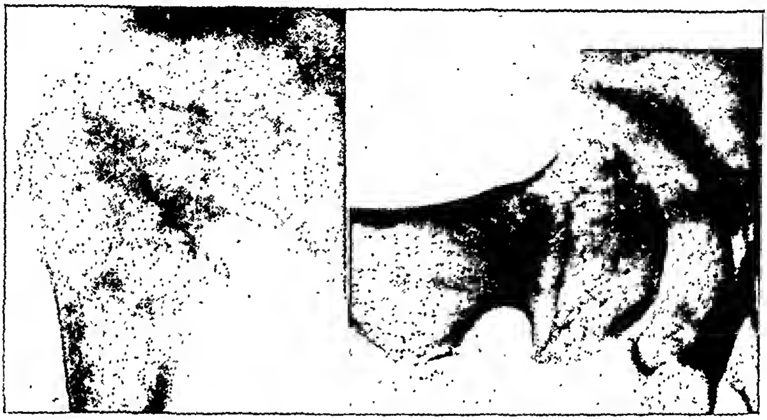


FIG. 6.—Pseudocoxalgia healed with deformity: flattening of head, coxa vara, retroversion.

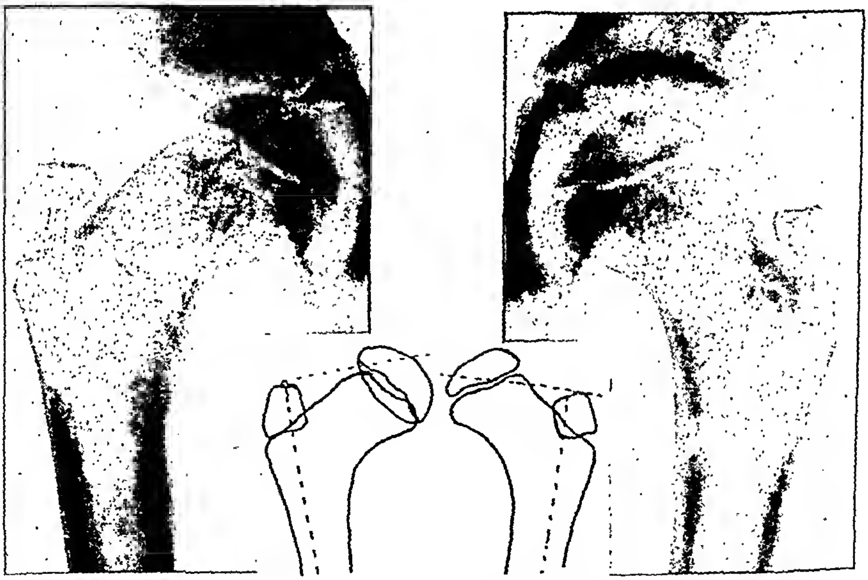


FIG. 7.—Boy, aged 8, no symptoms. Right epiphysis tilted, showing twofold lower contour. Tip of trochanter level with upper end of epiphyseal line.

Lantern slides were projected illustrating the treatment of (1) syndactyly by the free skin graft method; (2) flexion contracture of limbs following burns; (3) radionecrosis following treatment of large hæmangioma upper end of humerus; (4) loss of thumb; (5) chronic ulceration due to various causes.

Three cases were then shown.

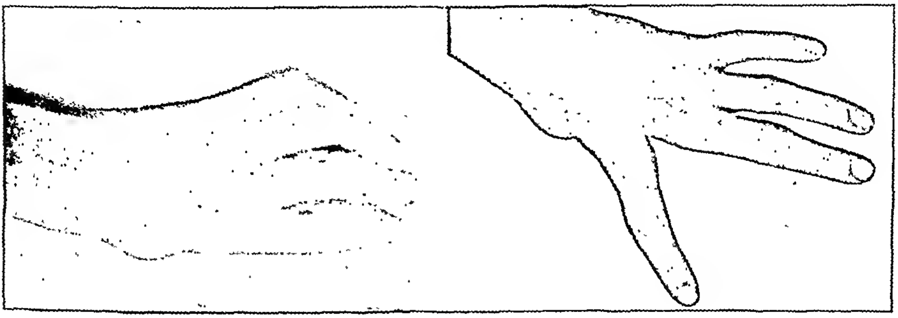


FIG. 1 A.

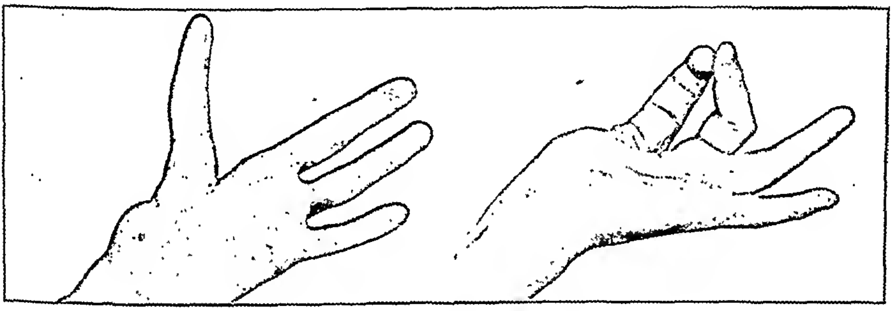


FIG. 1 B.

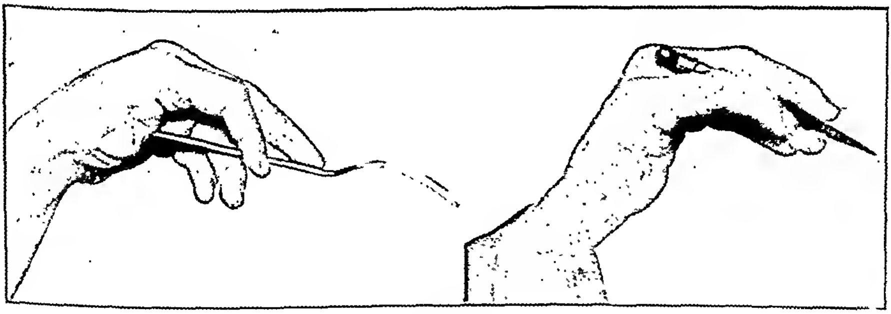


FIG. 1 C.

FIG. 1.—Case I. Loss of thumb. A. Before and after operation. B and C demonstrate functional result.

CASE I (fig. 1A, B, C).—T. R. First seen 18.2.39, nine months after accident. Electric burns, left forearm and hand. Fell over "Live rail" at Portsmouth. Thumb missing.

18.2.39: Operation, Treloar Hospital, Alton. Operation following Lambrinudi technique. Cleft between index and ring fingers deepened by free skin graft on stent mould. Oblique osteotomy (Mr. Langston) middle of shaft of metacarpal through separate incision on radial side. Fixation in plaster of Paris.

21.6.47: Patient, now 17 years old, demonstrates excellent function: was left-handed before injury: now writes with right hand but can do so equally well with left. Uses cup or tumbler naturally.

[*June* 21, 1947]

Brief Note on the Contributions of the late Sir Henry Gauvain to Orthopædic Surgery

Sir Thomas Fairbank said that Sir Henry Gauvain was appointed to the Lord Mayor Treloar Hospital, Hants, in 1908; he was, from the first, an ardent advocate of conservative versus operative treatment for non-pulmonary tuberculosis, and the aspiration of tubercular abscesses instead of incision. Gauvain insisted on the paramount importance of general treatment, in addition to local, and did pioneer work in the use of heliotherapy, open air, sea-bathing and light treatment. He insisted on "lessons" and occupational therapy to fill the patients' time.

A college was opened for teaching a trade to crippled lads, and so enable them to earn a living. He advocated the use of celluloid splints, rendered non-inflammable by a special method, for selected tubercular and other cases. The plans for rebuilding the hospital were largely the result of his experience and thought. He published valuable instructions for the use of the iron lung. His test for the activity or quiescence of tubercular arthritis of the hip (*Lancet*, 1918 (ii), 666) has proved of the greatest value. Lastly his exceptional personality and its great influence on the staff and patients was referred to.

A full account will be published in the *Journal of Bone and Joint Surgery*.

Cases and Case Records Illustrating Orthopædic and Plastic Surgical Team Work

By Professor T. POMFRET KILNER, C.B.E., F.R.C.S.

IN the early twenties, Sir Henry Gauvain invited Sir Harold Gillies and me to pay occasional visits to the Lord Mayor Treloar Hospital to carry out reconstructive work on cases of lupus in which the original disease and its curative treatment had produced deformity or disfigurement.

As the incidence of lupus in children became less frequent, the call for plastic surgical treatment of this kind diminished but a wider definition was given to the word "cripple" by the Trustees and when London hospitals became unpleasant residences for children in the early days of the war I was privileged to transfer to Alton my waiting lists of all cleft lip and palate cases from St. Thomas's Hospital and the then Princess Elizabeth of York Hospital for Children, Shadwell. Many of these cases requiring secondary corrections of a non-urgent character are still waiting for treatment, for Hampshire became "cleft lip and palate minded" and we now have a County service for these conditions run by the Medical Officer of Health to whom all cases are notified and who arranges for them to be seen either at the local Orthopædic Clinics or here. The follow-up system for these cases is excellent.

More than 90% of our work now consists of such cases and can be of little interest to the orthopædic surgeon. The other 10% is concerned with the treatment of congenital and acquired defects of the limbs. In most instances we are called upon to supply skin in the form of free grafts to parts where this is congenitally missing or has been lost by trauma, or to replace unstable scarred areas by sound full-thickness flap skin to allow orthopædic procedures to be carried out in comfort and without danger of infection to deeper structures.

CASE II (fig. 2A, B).—P. W., born 26.11.39. Syndactyly, left hand and both feet.

1.8.42: Operation, Treloar Hospital, Alton. Fingers separated. Fingers splinted in abducted position. Thickish Thiersch graft from left thigh applied on stent mould to raw surfaces.

CASE III (fig. 3).—R. G., born 4.5.43. At 6 months scalded with hot-water bottle. Extensive scarring right side trunk extending to axilla, groin and outer side right thigh.

Arm abducts to less than 90 degrees. Limitation of extension of right hip.

2.9.44: Consultation at Treolar Hospital, Alton. *Advice*—X-ray therapy; later, free the contracture, and graft. Three applications X-rays at Warren Road, Guildford.

6.10.45: Operation, Treloar Hospital, Alton. Scarred area across right groin incised and margins allowed to retract. Extended position of hip produced very large raw surface. Thiersch graft in four pieces applied to raw area from same thigh. Flavine emulsion gauze graduated compress. Spica.

20.10.45: All grafts taken well.

5.1.46: Incision across axilla at upper border of scar: Thiersch graft from left thigh. Pressure dressing held by tie-over silk stitches. Crepe bandage: plaster fixation in abduction.

19.1.46: Good take of graft.

21.6.47: Child now exhibits no disability. Grafted areas are sound and supple and all movements are free..

The Brittain Method of Arthrodesis of the Hip

By H. H. LANGSTON, F.R.C.S.

THIS paper is based on a series of 28 cases in which by this method an extra-articular arthrodesis of the hip has been attempted. Apart from Brittain's own cases, the only other recorded groups of cases have been published in America by Knight and Bluhm and by Freiberg.

In 25 cases the operation was performed on patients in whom the hip-joint had been disorganized by tuberculous disease. In three cases the hip was the subject of an advanced or painful osteo-arthritis. Of the 25 T.B. cases, 4 were operated upon before their tenth birthday, 20 were between 10 and 16 years of age and one was a doctor aged 28. There were three cases only in these series for whom the operation was carried out for osteo-arthritis; all three were between 50 and 55 years of age. In two cases bony union was secured. In one case bony union was not obtained, but this patient has been seen recently—four years since operation—and has remained completely free of pain. She has 30 degrees of flexion movement.

In 22 patients sound bony arthrodesis has been obtained. In five, bony union across the hip-joint extra-articularly has not been achieved. One case is too recent for the outcome to be known.

This method of arthrodesis is attractive for the following reasons:

(1) If correctly carried out, a graft bridging the hip-joint can be inserted from femur to ischium well away from the hip-joint as a truly extra-articular procedure.

(2) The graft is also usually well away from any extension of disease from the hip into the bony pelvis as extension downwards into the ischium is less frequently encountered than upward extension of the disease in the ilium. The operation is particularly suitable for cases in which extension of disease in the ilium has produced the so-called "wandering acetabulum".

(3) The method allows of the simultaneous correction of any deformity present at the hip as the result of the disease instead of this deformity having to be corrected at a subsequent operation as is the case in the majority of ilio-femoral methods of arthrodesis.

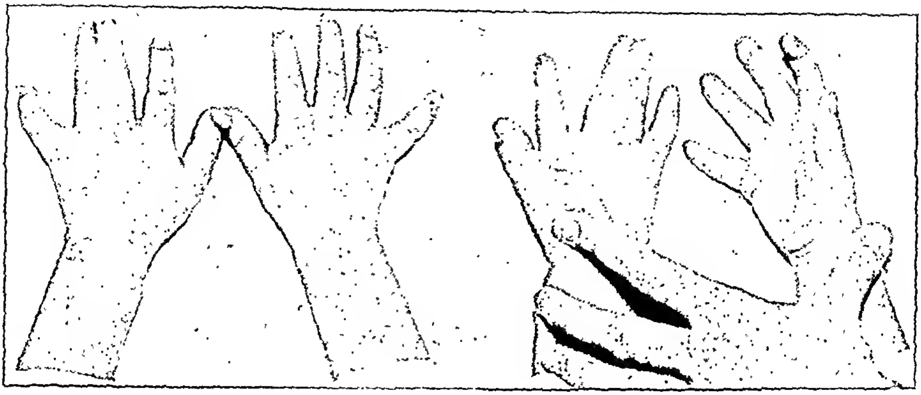


FIG. 2 A.

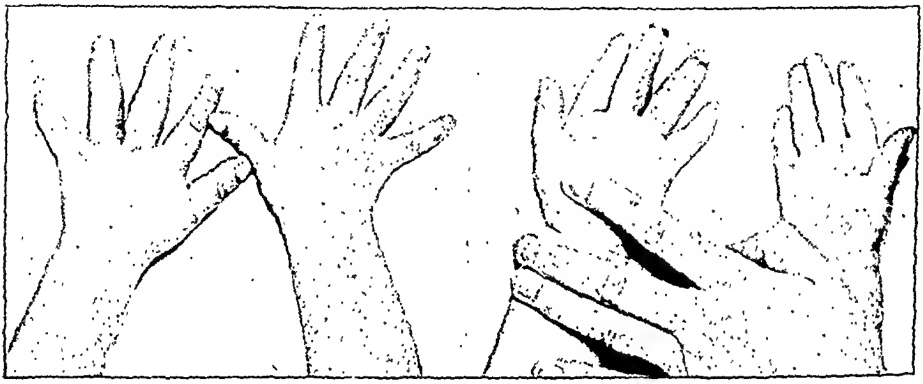


FIG. 2 B.

FIG. 2.—Case II. Congenital syndactyly. A before and B after treatment by skin-graft operation.

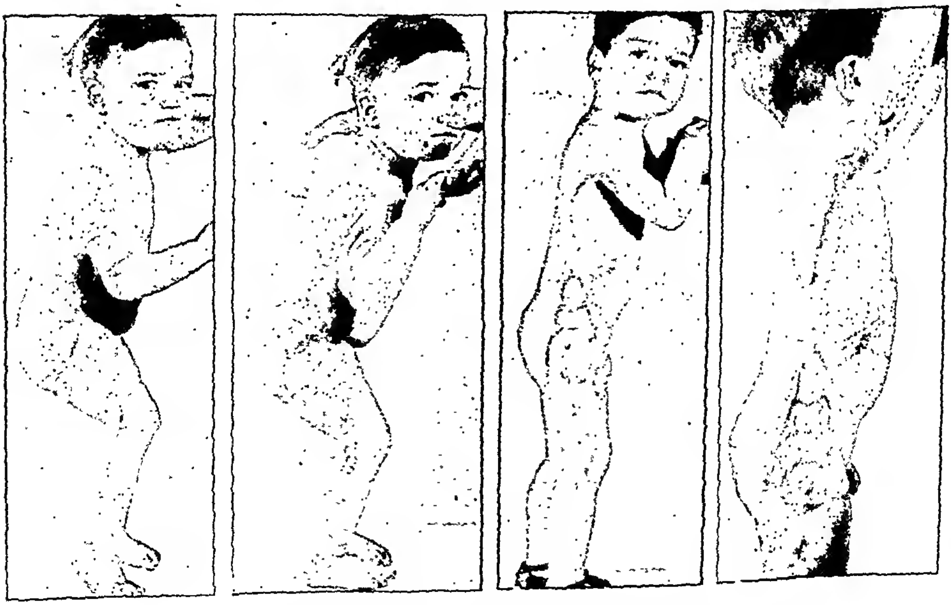


FIG. 3.—Case III. Severe burn contractures treated by free skin grafts.

CASE II (fig. 2A, B).—P. W., born 26.11.39. Syndactyly, left hand and both feet.

1.8.42: Operation, Treloar Hospital, Alton. Fingers separated. Fingers splinted in abducted position. Thickish Thiersch graft from left thigh applied on stent mould to raw surfaces.

CASE III (fig. 3).—R. G., born 4.5.43. At 6 months scalded with hot-water bottle. Extensive scarring right side trunk extending to axilla, groin and outer side right thigh.

Arm abducts to less than 90 degrees. Limitation of extension of right hip.

2.9.44: Consultation at Treolar Hospital, Alton. *Advice*—X-ray therapy; later, free the contracture, and graft. Three applications X-rays at Warren Road, Guildford.

6.10.45: Operation, Treloar Hospital, Alton. Scarred area across right groin incised and margins allowed to retract. Extended position of hip produced very large raw surface. Thiersch graft in four pieces applied to raw area from same thigh. Flavine emulsion gauze graduated compress. Spica.

20.10.45: All grafts taken well.

5.1.46: Incision across axilla at upper border of scar: Thiersch graft from left thigh. Pressure dressing held by tie-over silk stitches. Crepe bandage; plaster fixation in abduction.

19.1.46: Good take of graft.

21.6.47: Child now exhibits no disability. Grafted areas are sound and supple and all movements are free.

The Brittain Method of Arthrodesis of the Hip

By H. H. LANGSTON, F.R.C.S.

THIS paper is based on a series of 28 cases in which by this method an extra-articular arthrodesis of the hip has been attempted. Apart from Brittain's own cases, the only other recorded groups of cases have been published in America by Knight and Bluhm and by Freiberg.

In 25 cases the operation was performed on patients in whom the hip-joint had been disorganized by tuberculous disease. In three cases the hip was the subject of an advanced or painful osteo-arthritis. Of the 25 T.B. cases, 4 were operated upon before their tenth birthday, 20 were between 10 and 16 years of age and one was a doctor aged 28. There were three cases only in these series for whom the operation was carried out for osteo-arthritis; all three were between 50 and 55 years of age. In two cases bony union was secured. In one case bony union was not obtained, but this patient has been seen recently—four years since operation—and has remained completely free of pain. She has 30 degrees of flexion movement.

In 22 patients sound bony arthrodesis has been obtained. In five, bony union across the hip-joint extra-articularly has not been achieved. One case is too recent for the outcome to be known.

This method of arthrodesis is attractive for the following reasons:

(1) If correctly carried out, a graft bridging the hip-joint can be inserted from femur to ischium well away from the hip-joint as a truly extra-articular procedure.

(2) The graft is also usually well away from any extension of disease from the hip into the bony pelvis as extension downwards into the ischium is less frequently encountered than upward extension of the disease in the ilium. The operation is particularly suitable for cases in which extension of disease in the ilium has produced the so-called "wandering acetabulum".

(3) The method allows of the simultaneous correction of any deformity present at the hip as the result of the disease instead of this deformity having to be corrected at a subsequent operation as is the case in the majority of ilio-femoral methods of arthrodesis.

(4) Brittain is correct in his contention that as this is a method by which a graft is inserted in compression (as opposed to the tension on the ilio-femoral graft) union in a successfully placed graft is remarkably rapid and solid. Even if bony fusion by graft fails, a satisfactory clinical result may follow from the fact that one has carried out a bifurcation osteotomy. Sir Henry Gauvain showed many years ago that a satisfactory firm fibrous ankylosis and sometimes bony ankylosis could be achieved by this osteotomy alone.

(5) The removal of the pull of the adductors on the hip by the osteotomy is a further advantage and in itself (as Wilkinson has shown) may lead to a rapid alteration and improvement in the radiological appearance of the hip. This was well illustrated in some of these cases.

(6) In this operation no extensive stripping of muscle is necessary and although hæmorrhage and shock need not be a problem in these days, in methods necessitating a Smith-Petersen approach, there is less risk of shock in this method.

(7) Although I advise waiting until a child is at least 10 years of age before carrying out this operation, it has been done with success in a somewhat puny boy of 8, whose home conditions were such that it seemed unlikely that parental care would be good, and that therefore instructions as to protective appliances might not be carried out. I think most orthopædic surgeons feel that an ilio-femoral arthrodesis under 10 to 12 is a somewhat uncertain procedure.

The operation has, however, certain practical difficulties and disadvantages which are not yet fully solved:

(1) The method of insertion of the graft into the ischium is blind. The ischium itself is never exposed and seen. X-ray control of the line of osteotomy is of assistance, but the ultimate making of the cleft in the ischium is blind, and one is entirely dependent on a sense of touch at the end of an osteotome together with such guidance as anatomical points can provide to guide one in the correct line.

(2) The sciatic nerve, lying on the posterior aspect of the obturator internus, gemelli and quadrator femoris, although in a measure protected by these muscles, is probably not much more than ½ in. behind the line which the graft and, still more important, the osteotomes, traverse on the way to the ischium. In a case in which there is any marked degree of flexion deformity present, the nerve may be in serious danger.

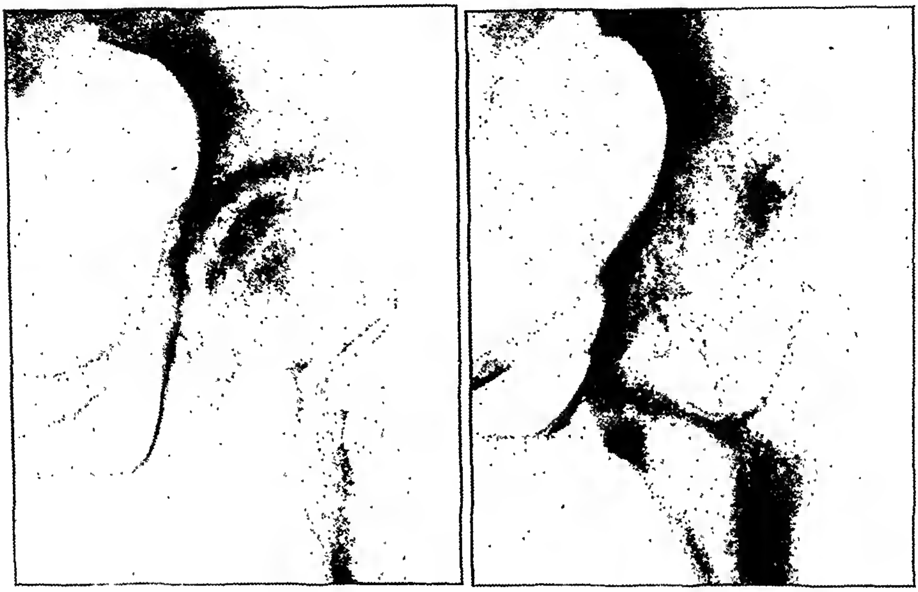
Although in this series of 28 cases there has never been the slightest suggestion of damage to the sciatic nerve, one orthopædic surgeon has told me of a personal case in which a sciatic paralysis was found the day after operation and exploration of the nerve revealed that the graft had transfixed the nerve on its way to the ischium.

(3) I have also been told of a case in which the graft was directed too far anteriorly, apparently into the ilio-pubic ramus through which it passed to perforate the external iliac artery.

(4) Although if the osteotomy is correctly planned and the femur clearly divided without splintering it is not difficult to find the ischium and drive an osteotome into it, it is often much more difficult to make the thicker and softer graft enter the cleft in the ischium, which closes like an oyster once the osteotome is removed.

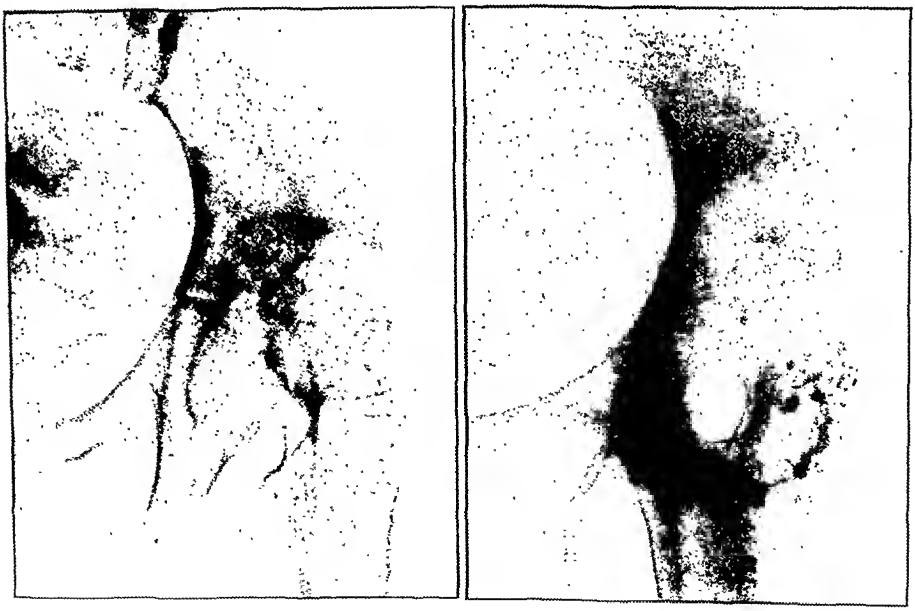
The five failures in this series were all due to this difficulty; in three the graft slipped upwards, possibly into the hip-joint, and in two the graft appears to have perforated the obturator foramen.

Special difficulty is likely to be encountered in cases of long-standing disease where growth of the pelvis has been retarded and the ischium is small and possibly obliquely placed.



A. B.

FIG. 1.—Tuberculous hip. Onset at 3 years of age, arthrodesis at 12½ years. A. Condition at 12½ years. B. Condition four years after arthrodesis.



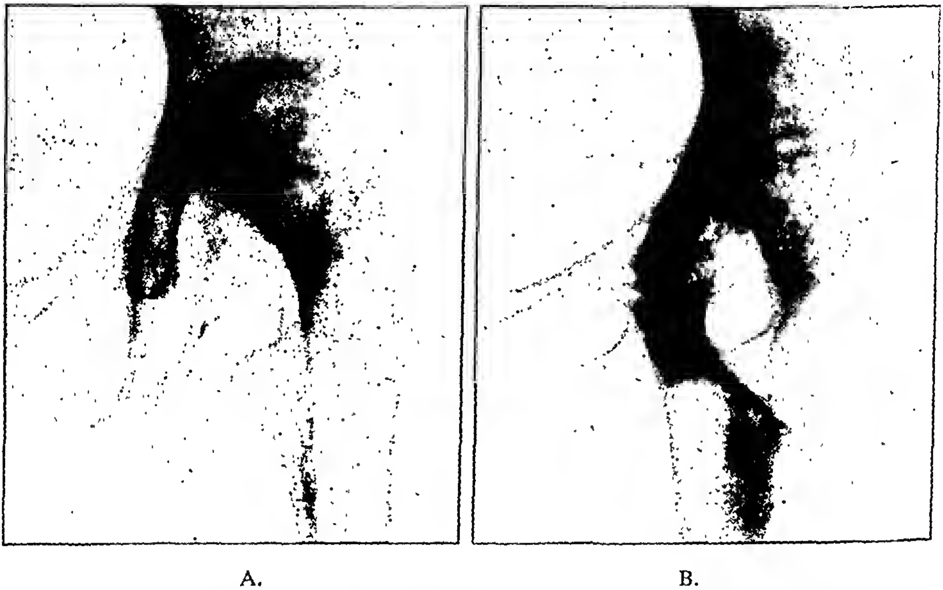
A. B.

FIG. 2.—Tuberculous hip. Onset at age of 7 years, arthrodesis at 14 years. A. Appearance before arthrodesis. B. Three years after arthrodesis.

A few points in technique seem worthy of mention:

(1) It is essential to make the osteotomy in the right line if the graft is to engage satisfactorily in the ischium. I always now therefore insert a Watson-Jones guide wire into the femur before carrying out the osteotomy, planning the line of osteotomy by the X-ray film taken of the hip immediately after insertion of the wire.

(2) The osteotomy must be an absolutely clean cut; any spike on the inner side will lead the osteotome and graft astray—usually into the hip-joint. It is wise therefore to begin one's osteotomy on the inner side, starting with a keyhole saw or the reciprocating blade of the Luck saw, and cut from within outward. This is not difficult if the incision is somewhat to the front of the femoral shaft, allowing a good view of the anterior aspect of the femur.



A. B.

FIG. 3.—Tuberculous hip. Onset at age of 8 years, arthrodesis at 13 years. A. Appearance before arthrodesis. B. Appearance three years after arthrodesis.

(3) Brittain advocates a massive graft including both the anterior and the posterior border of the femur. A wide graft is wise but I do not believe it is necessary to include the anterior and posterior borders, and although I have sometimes done so, my experience has been that it is rather more difficult to get such a graft to lodge securely in the ilium owing to its bulk.

SUMMARY

If the tibial graft can be made to engage correctly in the ischium a rapid and strong arthrodesis of the hip can be obtained by the Brittain method, and obtained at an early date. Even if arthrodesis is not obtained, a fair clinical result will follow from the fact that a bifurcation osteotomy is an essential part of the procedure. The route of approach to the ischium, however, involves risk of damage to important structures, and as far as I can see, no measure has yet been designed whereby this risk can be eliminated with any degree of certainty. The engagement of the graft in the ischium can be difficult, and failure may follow from the graft slipping upward towards the hip-joint or through the obturator foramen.

Section of Obstetrics and Gynæcology

President—JAMES WYATT, F.R.C.S., F.R.C.O.G.

[*June* 20, 1947]

DISCUSSION ON SOME RECENT DEVELOPMENTS IN KNOWLEDGE OF THE PHYSIOLOGY OF THE BREAST

Dr. S. Engel: *Histology of the lactating breast.*—It is common knowledge that physiological function depends on the capacity of an organ to respond to an adequate stimulus. In the case of the breast there is variability in the function of lactation; this may be due either to inadequate capacity of the breast or of lactogenic stimuli. A morphological study of a large number of breasts revealed that the breast does, in fact, show great individual variations in structure which are closely related to its functional capacity.

The methods of investigation were as follows: Sections through the whole breast were prepared, and these gave a good survey of mammary architecture. These sections were about 100μ thick. Thin sections cut from smaller blocks have been used for the investigation of finer details.

There are two features of mammary structure which have an important bearing on the capacity of individual breasts to react to hormonal influences. The first is the variation in the total amount of glandular tissue present in different breasts, and the second the degree of differentiation of this tissue.

First, the total amount of glandular tissue: Investigation of some 80 breasts showed that only 20% to 30% contained glandular tissue in the same abundance as animals such as cows, dogs, guinea-pigs, rabbits and others which were examined for comparison. 30% to 40% contained less than an average amount of glandular tissue. The remainder fell somewhere between these limits.

The percentage of breasts which anatomically appear capable of adequate lactation corresponds closely with that observed in clinical practice. The relationship is closer still when the time for which lactation is maintained is also taken into account.

The glandular tissue is chiefly concentrated at the periphery and in the base of the breast; there is seldom much in the centre.

The features I have described are more easily seen in the lactating than the resting breast as the glands are minute and difficult to study in the latter.

When the glandular tissue is deficient in quantity, the glands themselves are usually poorly differentiated.

In the resting breast, the alveolus is lined by two distinct layers of cells, whereas during lactation there is only one layer. French investigators believe that, during the transition from rest to activity, the large cells of the external layer are reduced to minute dimensions, and the cells of the internal layer become the secretory cells. They consider the reduced cells of the external layer correspond to the cells of Boll in the sweat glands. In my own experience, the external layer consists of large, pale, slightly irregular cells, and the internal layer of regular, small, columnar cells. The cells of the external layer are the precursors of the secretory cells, whereas those of the inner layer represent a kind of protective covering. This is deduced from the observation that shrinkage and desquamation of the cells of the internal layer take place at the very beginning of lactation, and the cells then appear in the colostrum. In the non-lactating breast, the protecting layer serves to retain any small amount of secretion which may occur in the resting breast during menstruation. The abundant peri-acinar lymphatics are the means by which any retained menstrual secretions are removed.

Do menstrual changes occur in the breast? Because of the natural variations in the glandular equipment of different breasts it can be said that there is no rule and menstrual changes may or may not occur.

In sections through breasts of women who died during various phases of the menstrual cycle it is seen that, when they contain an abundance of well-differentiated glands promising satisfactory lactation, there is some alveolar sprouting in the pre-menstruum. On the other hand, in breasts which contain only a few primitive glands, there is no evidence of any response to menstrual influences. Occasionally, there are islets of primitive alveoli in otherwise well-developed breasts, in these cases such islets remain unaffected, although the remainder of the breast shows quite obvious menstrual changes. There can be little doubt that the differences of opinion about the behaviour of the breast during menstruation are accounted for by individual variations in anatomy. More important, since only well-equipped breasts are capable of undergoing changes during menstruation, it is clear that consideration of the behaviour of the breast during menstruation affords an accurate means of predicting its capacity to lactate. It should be emphasized here that neither size nor palpation give any correct indication of the functional capacity of a breast.

Hormone therapy for failure of lactation.—In most cases the failure is due to the scarce and undifferentiated glandular tissue in the breast. In menstruation primitive glandular tissue does not respond to menstrual influences, and the hormones responsible for lactation cannot produce the immense amount of glands necessary for satisfactory lactation. It is, therefore, not surprising if the results of hormone therapy are not always encouraging; the most that can reasonably be expected is that, by these means, a poor breast can be made to secrete a little more for a little longer.

Finally, it has long been held that menstruation is injurious to lactation. The total daily secretion of a number of women was measured by the usual method of test-feeding, and it was found that the relationship between menstruation and lactation was exactly the reverse. Menstruation commenced only when the milk supply had already begun to fail.

Dr. S. K. Kon and Dr. Elinor Huntsman Mawson (*National Institute for Research in Dairying, University of Reading*): *Studies of certain vitamins and other constituents of human milk.*—This short paper deals with some of the salient points arising from an investigation, still unpublished, which lasted for four years and during which more than two thousand samples of milk were examined. The constituents estimated included vitamin A, carotenoids, vitamin B_1, riboflavin, ascorbic acid, fat, total solids and, in a small proportion of samples, lactose, total nitrogen, calcium and phosphorus. Particular attention was paid to the vitamins since less was known about them than about the major constituents of human milk.

The purpose of our investigation was to determine to what extent the vitamin content of milk reflects the state of nutrition of the mother with regard to these factors and to study the influence on the composition of milk of dietary changes brought about by wartime conditions. Owing to the food policy of the Government some of these changes were for better rather than for worse. Since food habits of different populations vary, as, for example, in urban and rural areas, we arranged to study the composition of milk obtained from more than one locality.

The collection of samples from large numbers of women in rural areas was obviously not feasible but Reading, a prosperous town in the centre of an agricultural area, provided a good starting point. It had the additional advantage of being close to the National Institute for Research in Dairying where the investigation was carried out. Regular collection of samples in Reading was begun in the early summer of 1941 and continued until March 1945. In April 1942 financial support from the Medical Research Council ensured continuance of the Reading investigation and enabled us to extend our activities to Shoreditch where samples were collected for us through the kindness of the Medical Officer of Health and his staff. This small section of a great urban area provided a good contrast to Reading. The population of Shoreditch is essentially of the working class, whereas in Reading samples were obtained from most sections of the community—from the wives of business and professional men as well as from those of industrial workers and of some farmers and agricultural labourers. The husbands of many women in both areas were, of course, in the armed forces. During the war Shoreditch was exposed to enemy attack to a much greater degree than Reading.

To compare results it was necessary to learn to what extent the composition of milk was influenced by factors other than diet. Such factors include the time of day, the stage of lactation, milk yield, the age and parity of the mother.

To study the composition of milk in early lactation a special series of samples was obtained from Paddington Hospital through the kindness of Dr. G. M. Gray and Professor

W. C. W. Nixon. We can mention only very briefly those aspects of these findings relating to work which we will describe in greater detail.

FAT

The fat content is particularly difficult to determine on account of the sampling errors to which it is subject. Those who have obtained human milk by manual expression will have noticed that at first it is blue and watery but as the breast is emptied it becomes more and more creamy in appearance. Chemical analyses confirm that the first milk is poor in fat while the strippings are very rich. When samples are to be examined for fat all the milk in the breast should be obtained but in practice it is not always easy to determine whether or not the breast has been completely emptied.

The fat content of milk is also influenced by the interval elapsing since the baby's last feed. It is obvious that samples taken immediately after feeding will be very rich in fat. As the interval after feeding increases the fat content decreases. Thus the fat content of samples taken at 6 a.m. is less than that of samples taken during the rest of the day. Studies of fat content would be best carried out on a complete expression of all milk secreted during twenty-four hours but as this is rarely practicable we have used a standard procedure of obtaining milk during the morning from breasts used four to six hours previously. We realize, however, that, owing to the difficulty of ensuring complete emptying of the breast, our results are not free from sampling errors.

The fat content of Shoreditch samples proved less than that of Reading samples. We are unable to give an explanation for this but in view of the difficulties just discussed it is doubtful whether the difference is of nutritional significance.

VITAMIN A AND CAROTENOIDS

Results obtained for vitamin A and carotenoids, which are fat-soluble, naturally vary with the fat content and when this is in error they will also be incorrect. In considering results for groups of women we have therefore preferred to express our values for these constituents in terms of concentration in the milk fat. This cannot be done for individual women, however, on account of individual variations in fat content.

In early lactation the vitamin-A and carotenoid content of milk fat, high at first, decreases rapidly. This is well known, especially for carotenoids since it can be observed visually. In later lactation the carotenoids soon reach a steady level but the vitamin A continues to decrease though more slowly. As our samples were taken at different stages of lactation it was necessary to introduce a correction for this before making comparisons. This was done in calculating the yearly mean values for Reading and Shoreditch. During the course of our investigation the vitamin-A content of the fat of milk samples from Reading remained unchanged. From a dietary point of view this was expected since the amount of preformed vitamin A available for consumption by nursing mothers did not alter greatly during this time. A special cod-liver oil supplement was given to pregnant women early in 1943 but this did not affect the vitamin-A content of the milk they later produced. On the other hand, the mean vitamin-A content of the milk fat of 41 Reading women who took supplements of vitamin A during lactation was significantly higher than that of all samples examined. The vitamin-A content of milk fat from Shoreditch women in 1942–3 and 1943–4 agreed well with that found at Reading but in 1944–5 there was a very appreciable drop for which we have been unable to find a dietary explanation. At the same time there was a less marked fall in carotenoids.

It should be mentioned that the carotenoids of human milk consist largely of xanthophylls and other pigments with little or no vitamin-A activity so that from a nutritional point of view they are almost negligible.

Those who are familiar with the marked seasonal variation in the vitamin-A content of cow's milk may be interested to know that no comparable change took place in our experience with human milk. There was, however, a seasonal difference in carotenoid content.

VITAMIN B_1

The vitamin-B_1 content of milk undergoes a marked change in early lactation. It is very low to start with and increases rapidly to the fifth week after which it remains more or less steady. It is obvious that results for early lactation samples cannot be compared with those for mature milk and in making comparisons we have used only samples taken from the fifth week onward.

In 1941 when our Reading investigation was begun, white bread was still on the market and it was not until April 1942 that the national wheatmeal loaf superseded it. The increase in the amount of vitamin B_1 in the national diet resulting from this change was accompanied by a proportionately smaller though significant increase in the vitamin-B_1

content of Reading milk samples. Unfortunately there were no Shoreditch results for the period in which white bread was consumed but the mean values for subsequent years were similar to those from Reading.

RIBOFLAVIN

The riboflavin content of milk, like the fat content, is subject to sampling errors. This is because the ingestion of riboflavin by the mother is rapidly followed by a rise in the riboflavin content of the milk. Samples taken at 6 a.m. give a low result because they are little influenced by meals and higher results are found for samples taken later in the day. Collection of all milk secreted during twenty-four hours, if possible, would be most suitable for the measurement of riboflavin but even then it would be important to ensure that on the day of the test no food rich in riboflavin and not normally consumed is included in the diet. As samples taken at 10 a.m. from breasts used four hours earlier give results which are roughly the same as the mean for the whole day we have used this procedure as the only possible one for making our comparisons.

The riboflavin content of milk from Reading and Shoreditch women remained almost constant during three years. The Reading values were consistently higher than the Shoreditch ones but the difference, although statistically significant, was not very marked. We prefer not to lay too much stress on it since the possibility cannot be excluded that the riboflavin content of breakfasts at Reading was higher than at Shoreditch and that Shoreditch women may have made up for this later in the day.

VITAMIN C

Before our investigation was begun there was already a considerable amount of published information about the vitamin C of human milk—almost all of it from other countries. We have confirmed previous findings that a high proportion of a mother's intake of vitamin C is secreted into her milk and that consequently lactation makes a considerable drain on her reserves. Just how seriously this should be regarded depends on one's views concerning the requirement of adults for vitamin C. At any rate Nature has made ample provision for the child and there seems to be little need for giving extra vitamin C to the breast-fed infant unless the mother is very poorly supplied with it, and even then the need of the mother will probably be greater than that of the child.

In July 1941 the vitamin-C content of milk from Reading was low but it rose rapidly and remained more or less at the higher level until December after which a marked fall occurred. The same trends were repeated at both Reading and Shoreditch in the following year. During these two years the country was largely dependent on native fruits and vegetables for vitamin C and the low values (2 to 3 mg./100 ml.) in January, February and March can be explained by a shortage of green vegetables and the seasonal decline in the vitamin-C content of potatoes. Oranges became available in March 1943 at Shoreditch and in April at Reading and doubtless accounted for the small rise observed in each case. In the early months of 1944 many more oranges came on the market and consequently the low levels of vitamin C observed in previous years were not repeated. Shoreditch values did not differ very greatly from those for Reading despite the fact that many Reading people grow their own vegetables.

TABLE I.—CERTAIN CONSTITUENTS OF MATURE MILK AT READING AND SHOREDITCH

Constituent	Locality	No. of samples	Mean value	Standard deviation
Fat*	R	612	4·78 g./100 ml.	1·47
	S	129	3·91 g./100 ml.	1·42
Solids-not-fat ..	R & S	1348	8·96 g./100 ml.	0·43
Lactose	R & S	516	6·94 g./100 ml.	0·34
Total nitrogen ..	R & S	522	0·213†–0·186‡ g./100 ml.	—
Calcium.. ..	R	76	29·9 mg./100 ml.	4·2
Phosphorus ..	R	76	13·0 mg./100 ml.	1·9
Vitamin A ..	R & S	1390	32·1§ i.u./g. fat	10·5
Vitamin D ..	R & S	pooled	0·2–0·4 i.u./g. fat	—
Vitamin B_1 ..	R & S	130	14·7 μg./100 ml.	3·3
	1941–2	363	16·0 μg./100 ml.	3·2
	to	361	18·5 μg./100 ml.	3·5
	1944–5	295	18·3 μg./100 ml.	3·3
Riboflavin§ ..	R	616	25·5 μg./100 ml.	7·0
	S	136	23·4 μg./100 ml.	5·9
Vitamin C ..	R & S	1499	3·54 mg./100 ml.	1·40

*Samples taken four to six hours after last feed; † at 5 to 8 weeks; ‡ at 21 to 24 weeks. § See text.

SUMMARY OF RESULTS

Table I gives a summary of our results for the composition of human milk. Values for the fat content are shown separately for Reading and Shoreditch because of the difference already mentioned. No general mean can be given for total nitrogen on account of the well-known change with stage of lactation. Values given are for the 5th to 8th, and 21st to 24th weeks. On the whole our results for the major constituents, which were obtained in collaboration with Dr. S. J. Rowland, agree well with those of other workers.

The value given for vitamin A has been corrected for the stage of lactation to represent that in the 17th week. No chemical method is available for vitamin D and the values given were obtained by Dr. K. M. Henry by biological tests. No general mean for vitamin B_1 can be given because of the change during our investigation but combined yearly means for Reading and Shoreditch are quoted instead. The riboflavin values used in obtaining the means were for morning samples as already described. The mean for vitamin C is based on a much larger number of samples as no special sampling precautions were needed.

An estimate of the amount of vitamins which a baby is likely to obtain from breast milk or from cow's milk shows that the breast-fed baby will get more vitamin A and vitamin C but much less vitamin B_1 and riboflavin.

DIETARY SURVEYS

It was of course of great interest to have information about the nutrient content of the diets of the women whose milk we examined. This was not possible on a large scale but three surveys were made for us at Shoreditch by Dr. H. M. Sinclair, by Dr. E. R. Bransby and by The Social Survey. All three gave very similar results. The diets of many of these women contained fewer calories and less calcium and vitamin A than is usually considered desirable for lactating women. The intake of calcium may have been higher than shown by the Surveys since it was not possible to take into account that obtained in the drinking water. Examination of the actual amounts of food consumed showed that full advantage was not taken of the extra allowances of foodstuffs for lactating women. Thus few women took more than one pint of milk daily whereas they could have had two pints if they had wished. It is clear therefore that our results for Shoreditch are representative of women consuming diets poorer in quality and quantity than wartime conditions warranted. Unfortunately dietary surveys were not possible at Reading so we have no data for comparison.

Our grateful thanks are due to all those people whose help made this investigation possible.

Dr. S. J. Folley (*National Institute for Research in Dairying, University of Reading*): *Recent researches on the physiology of mammary development and function.*—The first requisite for successful lactation is the existence of adequately developed mammary glands. This, in the last analysis, presupposes the presence of a sufficiency of histologically normal alveolar tissue, comprising the structural elements which synthesize milk constituents, in a functional condition. The presence of an adequate system of milk ducts, and, in animals such as the ruminants, gland cisterns, is also assumed. It is thus pertinent to begin a brief survey of recent work on the physiology of milk secretion with a consideration of mammary growth.

As is now well known, mammary growth is under the control of the ovarian hormones, œstrogen and progesterone. For the present purpose there is no need to consider the question whether these sex hormones act directly on the mammary tissues, or whether the ultimate effective agents are specific mammogenic hormones secreted by the anterior pituitary in response to stimulation by sex hormones, as claimed by Turner and his school. Unfortunately it is not possible to make any satisfactory generalization regarding the respective roles of œstrogen and progesterone in mammary growth, since experiments on various species have revealed quite striking species differences. We may, however, briefly summarize the main experimental findings as follows:

In some species, such as the mouse, rat, and rabbit, œstrogen alone, at any rate in physiological doses, evokes growth of the duct system but little or no alveolar development. In order to produce the latter, combined treatment with œstrogen and progesterone is necessary. In other species, of which a notable example which has long been familiar is the guinea-pig, œstrogen alone is capable of evoking the growth of duct and alveolar tissue alike. In short, it can develop a gland which, under suitable conditions, is able to produce considerable quantities of milk, as evidenced by the fact that male guinea-pigs, in which mammary growth has been brought about by treatment with œstrogen, will rear young. It has been claimed that the same is true for the monkey, though in this case all workers are not unanimous as to whether or not the amount of alveolar growth produced by œstrogen treatment, particularly in the male, is very extensive. The gland of the female monkey seems to be more responsive as far as alveolar growth is concerned.

content of Reading milk samples. Unfortunately there were no Shoreditch results for the period in which white bread was consumed but the mean values for subsequent years were similar to those from Reading.

RIBOFLAVIN

The riboflavin content of milk, like the fat content, is subject to sampling errors. This is because the ingestion of riboflavin by the mother is rapidly followed by a rise in the riboflavin content of the milk. Samples taken at 6 a.m. give a low result because they are little influenced by meals and higher results are found for samples taken later in the day. Collection of all milk secreted during twenty-four hours, if possible, would be most suitable for the measurement of riboflavin but even then it would be important to ensure that on the day of the test no food rich in riboflavin and not normally consumed is included in the diet. As samples taken at 10 a.m. from breasts used four hours earlier give results which are roughly the same as the mean for the whole day we have used this procedure as the only possible one for making our comparisons.

The riboflavin content of milk from Reading and Shoreditch women remained almost constant during three years. The Reading values were consistently higher than the Shoreditch ones but the difference, although statistically significant, was not very marked. We prefer not to lay too much stress on it since the possibility cannot be excluded that the riboflavin content of breakfasts at Reading was higher than at Shoreditch and that Shoreditch women may have made up for this later in the day.

VITAMIN C

Before our investigation was begun there was already a considerable amount of published information about the vitamin C of human milk—almost all of it from other countries. We have confirmed previous findings that a high proportion of a mother's intake of vitamin C is secreted into her milk and that consequently lactation makes a considerable drain on her reserves. Just how seriously this should be regarded depends on one's views concerning the requirement of adults for vitamin C. At any rate Nature has made ample provision for the child and there seems to be little need for giving extra vitamin C to the breast-fed infant unless the mother is very poorly supplied with it, and even then the need of the mother will probably be greater than that of the child.

In July 1941 the vitamin-C content of milk from Reading was low but it rose rapidly and remained more or less at the higher level until December after which a marked fall occurred. The same trends were repeated at both Reading and Shoreditch in the following year. During these two years the country was largely dependent on native fruits and vegetables for vitamin C and the low values (2 to 3 mg./100 ml.) in January, February and March can be explained by a shortage of green vegetables and the seasonal decline in the vitamin-C content of potatoes. Oranges became available in March 1943 at Shoreditch and in April at Reading and doubtless accounted for the small rise observed in each case. In the early months of 1944 many more oranges came on the market and consequently the low levels of vitamin C observed in previous years were not repeated. Shoreditch values did not differ very greatly from those for Reading despite the fact that many Reading people grow their own vegetables.

TABLE I.—CERTAIN CONSTITUENTS OF MATURE MILK AT READING AND SHOREDITCH

Constituent	Locality	No. of samples	Mean value	Standard deviation
Fat*	R	612	4·78 g./100 ml.	1·47
	S	129	3·91 g./100 ml.	1·42
Solids-not-fat ..	R & S	1348	8·96 g./100 ml.	0·43
Lactose	R & S	516	6·94 g./100 ml.	0·34
Total nitrogen ..	R & S	522	0·213†–0·186‡ g./100 ml.	—
Calcium.. ..	R	76	29·9 mg./100 ml.	4·2
Phosphorus ..	R	76	13·0 mg./100 ml.	1·9
Vitamin A ..	R & S	1390	32·1§ i.u./g. fat	10·5
Vitamin D ..	R & S	pooled	0·2–0·4 i.u./g. fat	—
Vitamin B$_1$ ..	R & S	130	14·7 μg./100 ml.	3·3
	1941–2	363	16·0 μg./100 ml.	3·2
	10	361	18·5 μg./100 ml.	3·5
	1944–5	295	18·3 μg./100 ml.	3·3
Riboflavin§ ..	R	616	25·5 μg./100 ml.	7·0
	S	136	23·4 μg./100 ml.	5·9
Vitamin C ..	R & S	1499	3·54 mg./100 ml.	1·40

*Samples taken four to six hours after last feed; † at 5 to 8 weeks; ‡ at 21 to 24 weeks. § See text.

recent experimental findings on galactopoiesis are thus presented as likely to be of interest to clinicians.

The discovery of the anterior-pituitary lactogenic hormone, by Stricker and Grueter (1928) and its subsequent characterization by Riddle and his collaborators as a pituitary hormone distinct from other pituitary hormones then known, and specific in its capability of causing growth and secretion of the pigeon crop-gland (a response now used for its biological assay), aroused interest in the possibility of stimulating lactation, particularly in cows and women, by anterior-pituitary extracts. With the development of methods for the partial purification of prolactin, methods which have been perfected to the point at which they now yield prolactin as a pure protein, there was some tendency to assume that purified prolactin preparations would prove more efficient as galactopoietic agents than unfractionated anterior-pituitary extracts. Extensive experiments on cows (*see* Folley and Young, 1940, 1945) have, however, shown that far from this being the case, unfractionated ox anterior-lobe extracts give considerably greater galactopoietic responses in cows in declining lactation, for a given unitage of prolactin as measured by the pigeon crop test, than partially purified prolactin preparations. Indeed, investigations on lactating cows with a series of anterior-pituitary extracts with various combinations of biological properties have revealed very little correlation between their respective prolactin (pigeon crop stimulating) and galactopoietic activities, though there was an interesting and fairly close relationship between the latter and the influence of these extracts on carbohydrate metabolism. In fact, the galactopoietic activity of anterior-pituitary extracts appears to be due to a complex of anterior-pituitary hormones, of which two important and essential members seem to be prolactin and adrenotrophin. With crude saline extracts of ox anterior pituitary, substantial, though temporary, increases in the milk yield of cows in declining lactation could be obtained, even in response to single subcutaneous injections. With repeated injections a more sustained, but still temporary, response is obtained.

In view of the fact that purified prolactin preparations have been and are being used for the treatment of hypogalactia in women, it may be of interest to consider the bearing of these experiments on cows on the clinical use of prolactin. Such clinical experiments with prolactin as have been reported have given variable and sometimes quite disappointing results. When it is remembered, however, that prolactin preparations for clinical use are standardized solely in terms of prolactin activity by means of the pigeon crop-gland response, the lack of unanimity on the efficacy of prolactin for the correction of hypogalactia is perhaps not surprising in view of the above-mentioned results in cows. This is quite apart from the fact that many cases of deficient lactation may not be due to under-secretion of pituitary hormones. It therefore seems logical to suggest that clinical trials should be carried out with crude saline extracts of ox anterior pituitary, similar to those which have been uniformly found (*see* Folley and Young, 1945) to give galactopoietic responses in cows, prepared under conditions which should ensure the presence in the extracts of all members of the galactopoietic complex of hormones. As has been pointed out, the lactating woman is surely more analogous physiologically to the cow in declining lactation than to the pigeon, and it would seem desirable that anterior-pituitary preparations intended for treatment of hypogalactia in woman should be assayed for galactopoietic activity by a mammalian test.

Finally, we may consider a further endocrine relationship, the study of which has resulted in the development of a galactopoietic agent which, on account of its cheapness and ease of preparation, will no doubt prove to be of considerable practical importance in the dairy industry. It should therefore be of interest to the clinician.

The thyroid gland by virtue of its well-established role as a regulator of body metabolism, might be expected to influence lactation in so far as the rate of milk synthesis by the mammary gland cells must tend, within limits, to increase as the metabolic rate increases.

Experiments on the effects of thyroidectomy on lactation have for various reasons given results which are difficult to interpret. Consideration of the relevant literature indicates that while lactation is possible in the absence of the thyroid, the milk yield is subnormal and the lactation period tends to be shortened.

The effects on lactation of administration of thyroid hormone are, on the other hand, less unequivocal. As long ago as 1896 Hertoghe, a Belgian clinician, observed a galactopoietic effect in a lactating cow as a result of thyroid feeding. Modern work on the subject dates from the experiments of Graham (1934) and since then numerous workers have confirmed the fact that feeding dried thyroid gland or injection of crystalline thyroxine causes a marked but temporary increase in the milk yield of lactating cows, which subsides after the treatment is discontinued. The main features of the galactopoietic effect resulting from thyroid treatment may be summarized as follows:

The increase in milk yield during the period of treatment is considerable and may (e.g. *see* Folley and White, 1936) amount to almost as much as 30% above the basal level. Over-

The most spectacular results coming under this category, however, have been obtained in ruminants. As far back as 1938, de Fremery showed that treatment with natural œstrogens would produce considerable udder development in virgin goats, and later experiments with synthetic œstrogens in our laboratory (e.g. *see* Folley and Malpress, 1944) and elsewhere have shown that not only in the virgin goat, but in the virgin heifer as well, suitable œstrogen treatment will cause the growth of udders capable in many cases of secreting economically important yields of milk. Most of these experiments were performed on goats and cows with intact ovaries, the possibility of the intervention of ovarian progesterone thus not being excluded. Sufficient experiments have now been done on ovariectomized ruminants to indicate, however, that successful results do not depend on the presence of the ovary, and we may therefore take it as an established fact that in the ruminant, œstrogen will bring about the development of both duct and alveolar tissues. The question whether the alveolar tissue so developed is normal in structure and amount is of course of prime importance, and will be dealt with in a moment. No satisfactory data exist for man, but if it is possible to argue by analogy with the monkey, it might be expected that in man also œstrogen alone would be capable of producing some alveolar development in addition to duct development.

As regards growth-promoting action on the mammary gland it was generally believed that progesterone alone was without effect. Recently, however, it has been shown that, provided large daily doses are given, growth of both ducts and alveoli can be obtained in the rat and mouse.

It is necessary at this point to turn to the consideration of functional aspects, since the lactational performance of an experimentally developed gland may depend, to a considerable extent, on the normality or otherwise of its histological structure. The main findings in extensive experiments on maiden heifers do indeed indicate the need for further morphological studies. The lactational responses, as measured by maximum daily and by total lactation yields of milk, varied widely among similar animals receiving identical or nearly identical treatment. Moreover, though the animals which responded best gave yields which can be considered as being of the same order as those which would have been expected from these animals had they become pregnant in the normal way, such responses were exceptional, and in general the response was not quantitatively comparable to a normal lactation. This at once raises the question of whether such experimentally developed glands are normal in structure, and it seems possible that some additional endocrine stimulus, the most obvious possibility being of course progesterone, acting in conjunction with the administered œstrogen, is necessary for the artificial development of glands capable of yielding amounts of milk such as would be obtained in a normal lactation.

And indeed, studies by Mixner and Turner (1943) on virgin goats indicated that the structure of the glands developed in response to œstrogen alone was abnormal in that the alveoli were excessively large in diameter, perhaps even cystic, and exhibited a tendency to papillomatous folding or puckering of the alveolar epithelium. On the other hand, in goats which received progesterone in addition to œstrogen, the mammæ were more normal histologically and the alveoli smaller in diameter. However, the histological technique used by these authors was hardly adequate for a critical study of the structure of large mammary glands. This question is now being investigated in our laboratory, in collaboration with Mr. K. C. Richardson, on a much more extensive scale with specially devised histological techniques involving, in particular, fixation by intravascular perfusion and collodion embedding and sectioning of the whole gland, the object being to probe more searchingly than hitherto the endocrine mechanisms involved in udder development in the goat. This investigation, which will utilize many expensive, specially bred goats, and very large quantities of progesterone, is as yet only in its preliminary stages, and all that can be said at present is that our findings confirm and considerably extend those of previous workers to the effect that the gland developed under the influence of œstrogen alone exhibits alveoli with excessively wide lumina, while combined treatment with œstrogen and progesterone in a ratio found to give optimal alveolar growth in experiments on small animals, gives a more nearly normal histological picture but sometimes a smaller gland.

So far in dealing with the function of the mammary gland, consideration has been confined to the phenomenon which we may describe as *lactogenesis*—the initiation of lactation. In the present state of knowledge and for clarity of discussion, it has been suggested (Folley and Young, 1940) that an allied but not necessarily identical phenomenon, the stimulation or augmentation of lactation already established, shall be described as *galactopoicsis*. It seems probable that the treatment of deficient lactation in women falls under this latter heading, since in most of such cases lactation has been initiated but the milk yield has failed to reach a level necessary for the adequate suckling of the infant. Some

JOINT DISCUSSION No. 3

Section of Obstetrics and Gynæcology with Section of Radiology

Chairman—JAMES WYATT, F.R.C.S., F.R.C.O.G.
(President of the Section of Obstetrics and Gynæcology)

[*May* 16, 1947]

DISCUSSION ON SOME ASPECTS OF SURGICAL AND RADIOLOGICAL TREATMENT OF CARCINOMA OF THE CERVIX

The Evaluation of the Results of Carcinoma of the Cervix Uteri Treated by Radical Vaginal Operation. [*Abridged.*]

By Professor SUBODH MITRA, F.R.C.S.Ed., F.R.C.O.G. (*Calcutta*)

During the Third International Radiological Congress in Paris (1931), when I submitted my five-year statistical end-results of carcinoma of the cervix uteri treated with radiation therapy, I found that Continental surgeons performing the radical vaginal operation in similar cases, and Adler of Vienna, by combining this operation with post-operative radiation, had obtained very satisfactory results. Although the general trend of opinion is in favour of radiation therapy for carcinoma of the cervix, the surgical treatment still occupies a definite place. Moreover, some workers who were previously converts of radiation therapy are coming back to surgery supplemented by post-operative radiation. An analysis of world statistics shows that whatever method be followed (operation or radiation), the end-results are, for all practical purposes, the same in the hands of experts. It has been proved beyond doubt by proper classification of cancer cases, and by obtaining data for operability rate, relative cure rate, absolute cure rate as well as by five-year and ten-year salvages that whatever method be applied, practically identical results are obtained with a small percentage of variation which may be a chance variation. It is the general belief that radiation therapy is much easier than surgery, but it is very difficult to check and control whether radiation therapy has been properly executed or not. Experts are of opinion that "properly performed radium therapy is as difficult to learn as the operation itself" (Adler).

In 1932 I started the radical vaginal operation supplemented by post-operative radiation.

Radical vaginal operation.—I have taken up the radical vaginal operation instead of the radical abdominal for the following reasons:

(1) The primary mortality is much less. Out of 151 patients operated on, 6 died, i.e. a primary mortality of 3·97% as against an average of 14% by the radical abdominal method.

(2) Stocky, plump and adipose patients can be more effectively tackled by the vaginal route.

(3) Complications of the nature of uretero-vaginal fistulæ are much less frequent after vaginal operation than after the abdominal. Even in the hands of some experts, this complication may occur to the extent of 12·3% after Wertheim's operation.

(4) The end-results after Wertheim's radical abdominal operation and Schauta's radical vaginal operation are practically the same. In my series there is 37·6% relative cure rate as against 39% of Bonney's series.

(5) The percentage of recurrence does not differ greatly after the two methods of operation, abdominal and vaginal. Kamniker, after making an extensive analysis of the materials of the 1st and 2nd Universitaets-Frauen Klinik in Vienna, has found 55% local and 30% glandular recurrences in Schauta's operation against 69% local and 26% glandular in Wertheim's operation.

(6) The greatest handicap to the radical vaginal operation is that cancer-affected lymph glands cannot be removed. It has been authoritatively worked out by Bonney, Taussig and others that there is glandular involvement in from 35–40% of all patients presenting themselves for carcinoma of cervix. Bonney claims that 23% of cases with gland involvement have passed through a five-year salvage, although the total relative cure-rate is 39%. Almost the same relative cure-rate has been found in my series of radical vaginal operation without removal of glands. Heyman's series give still better results (absolute cure rate

dosage with thyroid preparations leading to a condition of marked hypermetabolism may on the other hand decrease the yield. *Pari passu* with the enhancement of the milk yield, increases in both the percentages of fatty and non-fatty fractions of the milk solids have been observed. The increase in the non-fatty solids content is at the best slight and has not been uniformly reported; the fat content undergoes a more marked increase, however, sometimes to such a degree as to result in a 50% increase in the daily fat yield (Folley and White, 1936). These galactopoietic responses are slight or absent in cows treated during early lactation, and are most in evidence during the lengthy period of slow decline from the peak yield.

This work assumed importance from the point of view of wide-scale practical application in the dairy industry, when Ludwig and von Mutzenbecher (1939), following up the scattered observations of many earlier workers, showed that treatment of certain proteins, such as casein, with iodine under mildly alkaline conditions, produced iodoproteins which exhibited thyroid activity by the oral route, and from which thyroxine could be isolated after hydrolysis.

Since iodocasein can be made relatively easily from materials readily available it is evident
that we have here a cheap and plentiful
its activity is manif
to cows under prac

Large-scale exper
Research Council, a
with dried thyroid
protein. One impo
prolonged feeding o
above basal causes
losses in body-weigh
20% above basal),
compensation.

Clinical reports on hormones for the stimulation of lactation in women have not always been favourable. In fact, some clinicians have advocated thyroid treatment for the suppression of unwanted milk secretion! Nevertheless, in view of the large amount of information we now possess regarding the galactopoietic effect of thyroid preparations in cows, further clinical trials, keeping the necessity for careful control of dosage in mind, would appear to be justified.

REFERENCES

FOLLEY, S. J., and MALPRESS, F. H. (1944) *J. Endocrinol.*, 4, 1.
——, and WHITE, P. (1936) *Proc. roy. Soc. B*, **120**, 346.
——, and YOUNG, F. G. (1940) *J. Endocrinol.*, 2, 226.
——, ——, (1945) *J. Endocrinol.*, 4, 194.
DE FREMERY. P. (1938) *Arch. néerl. Zool.*, 3 (Suppl.), 48.
GRAHAM, W. R. (1934) *J. Nutrit.*, 7, 407.
HERTOGHE, E. (1896) *Bull. Acad. Méd. Belg.* (4me Série), **10**, 381.
LUDWIG, V., and VON MUTZENBECHER, P. (1939) *Hoppe-Seyl. Z.*, 258, 195.
MIXNER, J. P., and TURNER, C. W. (1943) *Res. Bull. Mo. agric. Exp. Sta.*, No. 378.
STRICKER, P., and GRUETER, F. (1928) *C. R. Soc. Biol. Paris*, **99**, 1978.

	TABLE III (1932-40)	TABLE IV (1937-40)	TABLE V (1932-36)
Total No. operated ..	93	40	53
5-year salvage	35	16	19
Relative 5-year cure rate ..	37·6%	40·0%	36·0%
Relative 10-year cure rate ..	—	—	24·5%

TABLE VI.—COMPARATIVE 5-YEAR CURE RATE DURING THE SAME PERIOD, 1932-1940

	Operation %	Radiation %
Stage I	61·5	66·0
Stage II ..	44·0	31·5
Stage III ..	15·6	12·6
Stage IV ..		2·3

	%
Absolute 5-year cure rate ..	12·9
Absolute 10-year cure rate ..	9·4

Unfortunately I cannot give an absolute cure rate of my cases from 1932 as the patients cannot be grouped under one particular method of treatment. Result will certainly be vitiated if an attempt be made to find out an absolute cure rate of operation cases against the bulk of remaining cases treated by radiotherapy.

My results from radiation therapy from 1926 to 1932 are as follows: the relative five-year cure rates are at 53·4% of Stage I, 37·5% of Stage II, 9·4% of Stage III, 1·7% of Stage IV. The absolute cure rate is at 12·9% after five years and 9·4% after ten years.

It is evident that the results of radiation are not so striking as those of operation. My hospital cannot afford to give free treatment to all cases thereby losing many early cases. The patients are mostly poor and irresponsible. 18·3% did not take the complete course of treatment either because they could not afford it or because they thought they were cured in spite of repeated warnings to the contrary. Moreover there being no arrangement for registration system, patients once changing their residence could hardly be traced. Follow-up is difficult as war, famine, flood and communal disturbances have dislocated civil life. If I take a relative cure rate of only those cases who have taken a complete course of treatment, the results will be 14·9%, which stands comparable with the results of other workers.

CONCLUSION

We have, as yet, got no remedy for advanced cases. Operable cases yield satisfactory results up to a certain limit whatever method is followed provided treatment be given efficiently and with meticulous precision. It is only by the detection of early cases and centralization of patients in special cancer clinics that we can markedly improve our end-results.

Mr. Charles D. Read (*London*): In any discussion on the subject of the treatment of carcinoma of the cervix, division of opinion invariably centres around the relative merits of radiation and radical surgery. This generally applies only to those cases coming within the category of stages one and two. There is agreement that almost all cases in stages three and four are unsuitable for treatment by radical surgery, though even in these cases it is possible to treat some by a combination of surgery and radiation.

We have various forms of treatment for carcinoma of the cervix by irradiation and surgery, and I submit that the correct method of treatment of any particular case is dependent upon the clinical features presented by the actual patient under consideration. Apart from the degree of advancement of the growth, its clinical type, the age of the patient, the presence of a cardiac or renal lesion, adiposity, and the general clinical condition of the patient, all constitute factors for careful consideration.

I have had no experience of the radical vaginal operation, having early dismissed it because of its neglect of attack on the gland-bearing area. Bonney has proved that in 40% of cases the glands are involved, so the Schauta operation cannot hope to benefit these cases. In addition gland involvement is irregular and does not depend on the degree of advancement of growth. However, I have had some experience with radiotherapy and with Wertheim's radical abdominal operation. My late chief, Mr. Victor Bonney, has, to date, operated upon over 500 cases, and can show a five-year survival rate of 40–43% following the Wertheim operation. With few exceptions he operated on all cases where removal of the growth was technically possible and of course this included many Stage 3 growths. His operative mortality was 14% over this series, and he did not combine radiotherapy with his operative measures.

On careful scrutiny of the results of any large series of cases treated either by irradiation or by radical surgical procedures, one is forced to ask "Could any of the unsuccessful irradiation cases have been saved by surgery?" and likewise, "Could any of the unsuccessful surgical

33·1%) without any surgical removal of glands. Schauta is of opinion that radical removal of glands is possible only in occasional cases; because when the iliac glands, which may be removed, are involved, the aortic group of glands, which are not surgically approachable are already carcinomatous. Some of the carcinomatous glands are bound to be overlooked because of their small size. Wertheim's opinion is that extirpation of the lymph glands can contribute nothing towards the improvement of end-results. According to Doederlein: "It is certainly more important in improving the operation for carcinoma, to extend the excision so as to take away the parametrial and paravaginal tissue with the uterus than to place too much hope for betterment in the extirpation of glands". The greater part of the lymphatic vessels infiltrated in a cervical carcinoma run with the uterine veins in the transverse cervical ligaments of Mackenrodt lying at the base of the broad ligament and extending from the uppermost part of the vagina and from the cervix to the lateral pelvic wall. When these lymphatic channels are infiltrated with carcinoma, cancer cells are well isolated from the rest of the body by the connective tissue sheath of the ligament. The spread of carcinoma is slow in this location because of the marked tissue-pressure. Once the cancer cells pass beyond the connective tissue bundle of Mackenrodt, they extend into loose subserous connective tissue: the prospects are no longer good, even if the lesion may be found operable from the technical point of view. But fortunately cancer cells remain shut up in Mackenrodt's ligaments for a considerable time and then spread slowly. This slow permeation is the reason why cervical cancer is a relatively favourable type of tumour for operation.

The logical conclusion naturally follows that in operations of cervical carcinoma, the most radical possible excision of the parametrial and paravaginal tissue should be made including also a wide cuff of vagina.

The abdominal route was preferred originally because great hopes were placed in the removal of the glands: the excision of parametrial tissue was never considered as important as the removal of lymphatic glands.

The surgeon, expert in vaginal technique and thoroughly conversant with the surgical anatomy of the pelvis, can remove a greater amount of parametrial, paravaginal, paravesical and pararectal connective tissue by the vaginal route with Schuchardt's incision than by the abdominal route. In my series, parametrium has been removed to the extent of about 2½ in. from each side.

(7) Lastly, the radical vaginal operation facilitates the introduction of radium in the parametrial tissue immediately or shortly after operation.

Professor Mitra next described the details of the technique of the extended vaginal operation. He then went on:

Post-operative complications.—Six patients died, the primary mortality being 3·97%; 3 patients died of shock, one of pulmonary embolism on the fourteenth day, one of pneumonia, and one of staphylococcal septicæmia.

The bladder was injured in 6 patients, of whom two required an operation for perfect recovery, whereas the fistula healed up spontaneously in 4 other cases. In 1 case the ureteric wall was so thinned out during dissection that it was almost on the point of bursting, but by careful stitching of the outer coat nothing untoward happened. In 3 cases there was injury to the rectal wall, due to a Schuchardt's incision, but it healed spontaneously. In 23% of the patients the perineal incision did not unite by first intention but later on healed by granulation.

B. coli infection occurs in about 54% of cases during the post-operative period. In 4 of my cases pyometra was present.

TABLE I

RECURRENCES AFTER OPERATION

After	Local	Glandular
Schauta's (vaginal) ..	55%	30%
Wertheim's (abdominal)	69%	26%

TABLE II

Operability rate	57·7%
Total No.	151
Primary mortality	3·97%
Relative 5-year cure	37·6%
Relative 10-year cure	24·5%

Statistical analysis.—For the assessment of statistical results three things are essential, viz. operability rate, relative cure rate and absolute cure rate. For the last twenty years I have been classifying my cases according to the League of Nation's formula and since 1932 operation has been undertaken as a side-chain to radiotherapy. Materials for operation were taken not only from Stages I and II but also from Stage III. Thus 42·6% of Stage I, 28% of Stage II and 5% of Stage III cases were operated upon and the rest were treated with radiation therapy. Patients were given a free choice and operation was performed only on willing patients although I have found out by careful scrutiny that 57·7% of all cases could have been operated on (*see* Tables II, III, IV, V, VI).

Results of Wertheim's Operation at the Chelsea Hospital for Women for the Years 1936-1941 Inclusive

	Stage 1	Stage 2	Stages 1 and 2
Number of cases treated..	34	20	54
Number alive at end of five years	14 — 41%	10 — 50%	24 — 44%
Lost in follow up	5	1	6
Number alive after five years excluding lost cases	14 — 48%	10 — 53%	24 — 50%
Operative deaths			3
Operative mortality			5·5%

Admittedly this is a very small series, but it does show that 54 consecutive Wertheim operations can be performed on Stages 1 and 2 cases by the various members of the staff with only three operative deaths. During the years 1936–1941 the cases for surgical treatment were not selected so conservatively as they are now, and in only relatively few cases was radiotherapy combined with surgery.

My own results of the combined approach are as yet too small in numbers and too recent in time to allow of useful analysis, but it is hoped at some later date to be able to show an improvement in the figures already shown.

I feel I must refer to the combined use of surgery and radiation in selected Stage 3 cases. On a number of occasions, after preliminary irradiation with the full Stockholm technique locally to the cervix, I have opened the abdomen, removed the appendages, and then performed a careful dissection of the iliac and obturator glands as in the Wertheim operation, but of course leaving the uterus in situ. This is followed by a full course of deep therapy. Time alone will assess the results, but to date the operative mortality has been nil.

The Radiological Treatment of Carcinoma of the Cervix Uteri

By G. E. Richards, M.D.
(*Director, Ontario Institute of Radiotherapy;
Professor of Radiology, the University of Toronto*).

Recently a number of writers on the subject of the treatment of cancer of the cervix have disparaged the use of radiotherapy and in the United States a number of surgeons have advocated a return to surgical methods. J. V. Meigs [1] has made the statement that "the treatment of cancer of the cervix by radiation is at a standstill". It may, therefore, be profitable to inquire how the best results obtainable by surgery compare with the best results obtainable by radiotherapy and whether the available evidence supports the statement that radiotherapy is static.

I. Comparison with Surgery

As has frequently been pointed out the work of Bonney in England and of Taussig in America provides, at least up to the present, the best results which have been attained by surgery. New methods of combating the post-operative complications of shock and infection may result in lowering the immediate death-rate following operation, but since the female pelvis does not lend itself to a true block dissection it will remain to be seen whether an improvement can be effected in end-results.

If a comparison is to be made of the results capable of being achieved by the two methods it is essential to compare the best results being secured by each. That this is not always done is evident from Meigs' paper already quoted in which, speaking of Taussig's operative results, the following statement is made: "Of 70 patients in Class II of the League of Nations Classification, 37% were living and well after five years. In a parallel group of 118 patients treated by radiation alone the five-year salvage was only 23%." The latter figure certainly does not represent the best results which may be secured by radiation, as will be shown presently. Bonney is reported to have operated upon 500 patients out of a total of approximately 900 diagnosed as cancer of the cervix. His five-year cure rate is stated to have been 40% for those in whom no glandular extension had occurred and 22% for those in whom lymph-node involvement was present—in other words, 40% for Stages I and II; 22% for operable Stage III cases. All Stage IV and a majority of Stage III were excluded from consideration, since they were not operated upon and therefore do not appear in the statistical report. The figures quoted for surgery in both cases represent the work of expert surgeons. It is important if a fair comparison is to be made that radiotherapy of an equally high standard be considered. For this purpose the figures from the recently published report from Manchester [2] may be used where it is reported that the five-year net survivals of cases treated in 1938 were as follows: Stage I 71%; Stage II 52%; Stage III 37%. Thus the average of Stages I and II which may be compared with Bonney's cases without lymph-node invasion is 54% against Bonney's 40%; and those in Stage III 37% against Bonney's 22%. Taussig's figure of 37% would have to be compared with the Manchester figure for Stage II of 52%.

cases have been saved by irradiation?'' Recurrences after either irradiation or radical surgery are notoriously disappointing in their treatment, and it is true to state that the time to treat a recurrence is before it has appeared!

Irradiation in the form of radium application and deep X-rays is applicable to the great majority of cases, but experience has shown that in some the growth appears to be radio-resistant, and after a preliminary healing, a breakdown occurs even after full irradiation. Koller's work on repeated biopsy during irradiation has shown that the radiosensitive and the radio-resistant growths can be fairly well distinguished during the comparatively early stages of radiotherapy. In like manner, it is accepted that the iliac and obturator glands vary in their reaction to the effects of deep therapy, and I can show specimens from patients on whom a Wertheim operation has been performed, following a full course of radium after the Stockholm method and succeeded by a full course of deep therapy, in which the cervix has healed perfectly, but in which the glands show active growth. The endocervical growth, whether columnar or squamous, appears to be particularly radio-resistant, and the presence of large fibroids or ovarian tumours, and especially of inflammatory disease of the appendages, contra-indicates radiation.

In the case of radical surgery, one is always up against the primary operative mortality, which of course cannot compare with the almost negligible risk of radiation. However, in a series of 500 cases, Bonney in his pioneer work had a primary operative mortality of only 14%—a truly remarkable tribute to his skill when it is recalled that he literally taught himself the operation and himself overcame all the difficulties which he has taught us to avoid, and he operated on practically every case that was technically possible. Recently we have had the advantages of routine blood and plasma transfusions, penicillin and the sulpha drugs, together with great advances in anæsthesia. These, together with the careful selection of patients for surgical treatment, can undoubtedly reduce the operative mortality to under 5%. In a series of over 200 consecutive Wertheim operations performed by my colleague Frank Cook or myself on Stage 1 and 2 cases only five patients failed to leave hospital or nursing home alive—mortality rate of 2·5%. It is not suggested that this figure is a tribute to exceptional operative skill. Indeed it is a tribute to the careful selection of cases for surgery, the judicious use of transfusion, the advance of anæsthesia and the care and co-operation of the nursing staff.

All my own cases had preliminary radiation in the form of at least one Stockholm dose of radium either seven days, or more, before operation, and the vast majority, about six weeks after operation, were subjected to a full course of deep therapy. In a few cases I have performed Wertheim's operation up to six months after full radiation by the Stockholm technique, and here again I can state that in the majority of such cases the operation had been made only slightly more difficult as a result of the preliminary irradiation. Pelvic sepsis is invariably the cause of the major difficulties.

The operation undoubtedly demands a reasonable degree of surgical competence, and should be completed within one and a quarter hours. After this time the condition of the patient deteriorates. Most of the cases selected are capable of completion in one hour, and many in under this time. The operator, I feel sure, should have served an apprenticeship with one who has had experience of the operation. Many appear to believe that the mortality rate is in the region of 25%—a completely fallacious figure in reasonably competent hands.

I submit that in our present state of knowledge, it is not in the best interest of the patient to embark on a fixed line of treatment by radiation or by surgery alone. Circumstances, in any case, may cause an alteration in the mode of attack. Generally speaking I feel that irradiation is the procedure of choice in the average case belonging to stages one and two. The following cases in these groups are, however, better treated by the Wertheim operation: (1) All endocervical growths. (2) Those in which biopsy shows radio-resistance. (3) Those in which ulceration recurs early after preliminary healing under irradiation. (4) Those in which the growth is complicated by the presence of large fibroids or ovarian tumours. (5) Those in which the growth is associated with pelvic inflammatory disease. (6) Where the patient refuses treatment by radiation. (7) Where the growth is in association with some congenital or acquired vaginal lesion making adequate irradiation impossible, e.g. vaginal stricture or double vagina.

Results of treatment.—In assessing the results of treatment, there is little doubt that a percentage of the patients who survive five years after irradiation are still literally dying of the disease due to the attenuated activity of the growth. A palpable mass or thickening in the pelvis of these patients is called ''fibrosis'' by the radiotherapy enthusiast, and ''growth'' by the surgical enthusiast. So often it is impossible to state dogmatically the true nature of this, and time alone makes the diagnosis certain one way or the other. I always feel that this tends to favour the figures showing the results of irradiation alone. After the radical surgical removal of a growth. the presence of a mass always signifies recurrence.

RESULTS OF WERTHEIM'S OPERATION AT THE CHELSEA HOSPITAL FOR WOMEN FOR THE YEARS 1936-1941 INCLUSIVE

	Stage 1	Stage 2	Stages 1 and 2
Number of cases treated..	34	20	54
Number alive at end of five years	14 — 41%	10 — 50%	24 — 44%
Lost in follow up	5	1	6
Number alive after five years excluding lost cases	14 — 48%	10 — 53%	24 — 50%
Operative deaths			3
Operative mortality			5·5%

Admittedly this is a very small series, but it does show that 54 consecutive Wertheim operations can be performed on Stages 1 and 2 cases by the various members of the staff with only three operative deaths. During the years 1936–1941 the cases for surgical treatment were not selected so conservatively as they are now, and in only relatively few cases was radiotherapy combined with surgery.

My own results of the combined approach are as yet too small in numbers and too recent in time to allow of useful analysis, but it is hoped at some later date to be able to show an improvement in the figures already shown.

I feel I must refer to the combined use of surgery and radiation in selected Stage 3 cases. On a number of occasions, after preliminary irradiation with the full Stockholm technique locally to the cervix, I have opened the abdomen, removed the appendages, and then performed a careful dissection of the iliac and obturator glands as in the Wertheim operation, but of course leaving the uterus in situ. This is followed by a full course of deep therapy. Time alone will assess the results, but to date the operative mortality has been nil.

The Radiological Treatment of Carcinoma of the Cervix Uteri

By G. E. RICHARDS, M.D.

(*Director, Ontario Institute of Radiotherapy;*
Professor of Radiology, the University of Toronto).

Recently a number of writers on the subject of the treatment of cancer of the cervix have disparaged the use of radiotherapy and in the United States a number of surgeons have advocated a return to surgical methods. J. V. Meigs [1] has made the statement that "the treatment of cancer of the cervix by radiation is at a standstill". It may, therefore, be profitable to inquire how the best results obtainable by surgery compare with the best results obtainable by radiotherapy and whether the available evidence supports the statement that radiotherapy is static.

I. COMPARISON WITH SURGERY

As has frequently been pointed out the work of Bonney in England and of Taussig in America provides, at least up to the present, the best results which have been attained by surgery. New methods of combating the post-operative complications of shock and infection may result in lowering the immediate death-rate following operation, but since the female pelvis does not lend itself to a true block dissection it will remain to be seen whether an improvement can be effected in end-results.

If a comparison is to be made of the results capable of being achieved by the two methods it is essential to compare the best results being secured by each. That this is not always done is evident from Meigs' paper already quoted in which, speaking of Taussig's operative results, the following statement is made: "Of 70 patients in Class II of the League of Nations Classification, 37% were living and well after five years. In a parallel group of 118 patients treated by radiation alone the five-year salvage was only 23%." The latter figure certainly does not represent the best results which may be secured by radiation, as will be shown presently. Bonney is reported to have operated upon 500 patients out of a total of approximately 900 diagnosed as cancer of the cervix. His five-year cure rate is stated to have been 40% for those in whom no glandular extension had occurred and 22% for those in whom lymph-node involvement was present—in other words, 40% for Stages I and II; 22% for operable Stage III cases. All Stage IV and a majority of Stage III were excluded from consideration, since they were not operated upon and therefore do not appear in the statistical report. The figures quoted for surgery in both cases represent the work of expert surgeons. It is important if a fair comparison is to be made that radiotherapy of an equally high standard be considered. For this purpose the figures from the recently published report from Manchester [2] may be used where it is reported that the five-year net survivals of cases treated in 1938 were as follows: Stage I 71%; Stage II 52%; Stage III 37%. Thus the average of Stages I and II which may be compared with Bonney's cases without lymph-node invasion is 54% against Bonney's 40%; and those in Stage III 37% against Bonney's 22%. Taussig's figure of 37% would have to be compared with the Manchester figure for Stage II of 52%.

Results in this institute.—Since 1929 there have been treated in this Institute 1,261 cases of cancer of the cervix, of which five-year figures are available in 756 cases. These results are shown in Table I indicating results similar to those quoted from Manchester. No doubt such figures are being obtained in most well-organized radiotherapy centres and provide a much more accurate figure for comparison than that quoted by Meigs.

TABLE I.—CARCINOMA OF THE CERVIX UTERI, 1929–1941

(*Net Survivals*)

		Living at end of					
Stage	No. cases	3 years		5 years		10 years	
I	80	67	83·8%	64	80·0%	29	72·5%
II	246	156	63·41%	132	53·66%	45	36·29%
III	289	105	36·33%	92	31·83%	23	20·90%
I, II and III	615	328	53·3%	288	46·83%	97	31·38%
IV	141	21	14·89%	13	9·22%	0	0%
Total All stages	756	349	46·2%	301	39·8%	97	29·1%

Average all cases:		
3-year survivals	349 of 756	46·2%
5-year survivals	301 of 756	39·8%
10-year survivals	97 of 333	29·1%
5-year survivals:		
Stages I and II	196 of 326	60·12%
Stage III	92 of 289	31·83%

In order to avoid misunderstanding the figures are given in the form of *net* survivals as in the Manchester report in Table I and also as gross survivals in Table II in which no deductions of any kind have been made.

TABLE II.—CARCINOMA OF THE CERVIX UTERI, 1929–1941

(*Gross Survivals—No Deductions*)

		Living at end of					
Stage	No. cases	3 years		5 years		10 years	
I	80	63	78·75%	57	71·25%	22	50·5%
II	246	150	60·98%	120	48·78%	36	29·03%
III	289	102	35·29%	84	29·06%	15	13·6%
I, II and III	615	315	51·22%	261	42·44%	73	26·25%
IV	141	17	12·06%	9	6·38%	0	0%
Total All stages	756	332	43·9%	270	35·71%	73	21·9%

Average all cases:		
3-year survivals	332 of 756	43·9%
5-year survivals	270 of 756	35·71%
10-year survivals	73 of 333	21·9%
5-year survivals:		
Stages I and II	177 of 326	54·29%
Stage III	84 of 289	29·06%

TABLE III.—CARCINOMA OF THE CERVIX UTERI

(*Comparison of Results by Surgery and Radiotherapy*)

	Stages I and II		Stage III	
	No cases	5-year percentage	No. cases	5-year percentage
Surgery:				
Bonney	500	40%	—	22%
Taussig	70	37%	—	—
Radiotherapy:				
Average of 9 clinics	2,233	41·4%	2,417	21·2%
Manchester 1934–38	340	45·2%	241	27·0%
Toronto 1929–41	326	60·12%	289	31·83%

It therefore seems a reasonable conclusion that radiotherapy is still superior to surgery by a substantial margin in those cases in which surgery is possible and has a very useful place in many cases in which surgery is quite impossible.

II

The second question in which we are interested is whether "the treatment of cancer of the cervix by radiation is at a standstill". A correct answer to this question should be equally interesting to gynæcological surgeons and to radiotherapists.

Table IV includes a tabulation quoted in full from Meigs' article, partly because it is an excellent compilation of figures from nine large clinics, both in Europe and America, but also because most readers will recognize the figures as being about fifteen years old and therefore as forming a suitable group for comparison with work of more recent vintage. Below have been added more recent figures from several centres representing present methods and results. On this basis it is apparent that quite substantial progress has been made in all groups except Stage IV. That an equally substantial improvement in the general average has not occurred may be explained by the fact that there is a widespread tendency to refer late cases to radiotherapy centres for the purpose of receiving palliative treatment and nursing care and the statistical tables are heavily and unfavourably weighted with such cases as a result. It is apparent in spite of this that definitely favourable progress has been made. The figures quoted would indicate an improvement up to 1938–40, of the order of 20% in Stage I; 15% in Stage II; 5–6% in Stage III and little or no change in Stage IV.

TABLE IV.—ANALYSIS OF RESULTS OF TREATMENT FOR CARCINOMA OF THE CERVIX

	Stage I		Stage II		Stage III		Stage IV		All stages	
Institution	No. of cases	% cured	No. of cases	% cured	No. of cases	% cured	No. of cases	% cured	No. of cases	% cured
Memorial Hospital (N.Y. City) ..	17	52·9	15	46·7	74	18·9	30	10·0	136	24·3
Women's Hospital (N.Y. City) ..	9	55·5	24	25·0	18	16·7	—	—	51	27·3
University of Brussels	6	33·3	20	40·0	28	14·3	9	0·0	63	22·2
Liverpool Radium Institute ..	8	62·5	28	25·0	43	14·0	15	0·0	94	19·1
Curie Institute (Paris)	9	66·6	20	60·0	75	20·7	22	4·5	126	33·3
Radium Centre (London) ..	4	25·0	27	11·1	37	18·9	19	0·0	87	12·6
Institut du Cancer (Paris) ..	9	44·4	15	53·3	40	35·0	19	10·5	83	33·7
Institut du Radium (Paris) ..	12	66·6	44	43·2	34	32·3	12	8·3	102	38·2
Radium hemmet (Stockholm) ..	31	48·4	67	26·9	71	8·5	42	9·5	211	20·4
All reporting hospitals	607	55·2	1,626	36·3	2,417	21·2	1,020	5·3	5,670	26·3
Recent figures										
*Marie Curie Hospital (London) 1945 Report	88	82·7	377	60·0	734	30·4	211	7·7	1,410	38·0
†Manchester—1945 Report (1934–38)	48	65·0	292	42·0	241	27·0	245	6·0	826	28·0
‡Toronto—1947 Report (1929–41)	80	80·0	246	53·6	289	31·8	141	9·2	756	39·8

*British Empire Cancer Campaign, Twenty-Second Annual Report, 1945, p. 34.

†Holt Radium Institute, Manchester, Second Statistical Report, 1934–38, Compiled 1945, "The Results of Radium and X-ray Therapy in Malignant Disease", p. 40.

‡ Figures quoted, also those from Marie Curie and Manchester, are "net" survivals. For "gross" Toronto survivals see Table II.

III

The next question is: "Can further improvements be looked for in the future?" We believe the answer is in the affirmative and that such improvements are to be found: (1) By an intensive campaign directed toward securing earlier diagnosis; (2) by improvements in the technical details of applying radium and its more skilful combination with roentgen therapy.

(1) *Earlier Diagnosis*

In most centres in which large numbers of cases are being treated it is still a discouraging fact that a majority of the cases being received for treatment are in the late stage when first seen. This in spite of fairly intensive educational campaigns designed to acquaint women with the symptoms of uterine cancer. We must, therefore, however reluctantly, conclude that this type of propaganda has failed up to the present and some new approach is urgently called for if we are to see more patients during Stages I and II when up to 75% of cures, or higher, may be expected. An effort to solve this problem has been under way in the United States for some years, where so-called "cancer prevention clinics" have been operated in New York and Philadelphia by Dr. Catherine MacFarlane. In these clinics patients having no reason to suspect the presence of cancer come for a physical examination at stated intervals. In her first 4,000 examinations Dr. MacFarlane is reported to have discovered two cases of cervical cancer, which low percentage would scarcely warrant the expense of setting up such clinics on a large scale.

The introduction of the Papincolaou smear method of cytological examination offers a method which can be carried out by the family doctor as a part of every physical examination, exactly as a urine and blood examination is now carried out.

Working under a grant from the Ontario Cancer Treatment and Research Foundation, Professor Edwin M. Robertson of Queen's University, Kingston, has conducted a trial of this procedure. Doctors throughout the district were provided with the necessary equipment and mailing tubes for containers. These containers hold a test tube with 95% alcohol, into which the discharge or fluid is injected by a special pipette. Sheets of instructions are supplied to each doctor and the containers are mailed in to the central laboratory. During the year 1946 Professor Robertson reports: "822 specimens of vaginal discharge were thus examined, and of this number two were found by this simple office procedure to be cancer, although the lesion was not visible to the naked eye on vaginal examination. The diagnosis was later confirmed by biopsy of the cervix. In 33 other cases of suspected or known cancer of the cervix (29) and uterus (4) the diagnosis was correctly made from the specimens sent in. In only one case was the diagnosis incorrect, but this specimen consisted almost entirely of blood and it was considered that the doctor had failed to observe careful technique in taking the specimen".

Here then is a simple office procedure no more difficult for the practising physician than a routine urinalysis and this test, as now carried out, has been proved to be 92% accurate, with the possibility of further improvement as experience is gained.

(2) *Improvements in Technical Details of Applying Radium and its More Effective Combination with Roentgen Therapy*

Several years ago we adopted the general principles described by Tod and Meredith in 1938 of calculating dosage with respect to those somewhat controversial Points A, B and S. We have modified the method slightly for our own use, but the chief difference has been in the routine use of roentgen therapy as a preliminary to the radium series. Since most of the lymph nodes in the pelvis lie close to the pelvic wall it is essential that a lethal dose for carcinoma be delivered at this point. Such a dose must be as close as possible to 5,000 r, which is not usually possible by means of radium alone in the form commonly employed, and not possible by roentgen therapy alone, short of excessive skin doses. Since 1938 the method used by us has included an intensive course of external irradiation by means of roentgen rays, followed by the radium series in three weeks' time. We believe there are advantages to be derived from the use of roentgen rays generated at 400 kV. as compared to 200 kV. in all cases except patients weighing not more than 120 pounds. A fuller discussion of this part of the subject has been published elsewhere (*Amer. J. Roentgenol.* In press). Table V gives the dosage which may be delivered at each of the important points within the pelvis. (Point C represents the side wall of the pelvis.)

TABLE V.—DOSAGE DELIVERED BY ROENTGEN THERAPY

No. of portals	Dosage in "r" (in air) per portal	Point A	Point B	Point C	Point S
6	1,800	2,970	2,970	3,150	1,870
6	2,100	3,460	3,460	3,660	2,180
6	2,400	3,960	3,960	4,190	2,490

Radium therapy.—In the past there have been several objections to the type of applicators available for the treatment of cervical carcinoma.

(1) *Inflexibility:* This criticism would be applied to metal applicators in which the intra-uterine and vaginal radium are combined, i.e. most T-shaped metal applicators.

(2) *Insecurity:* This is a very serious criticism and applies to corks, colpostats, boxes and almost all multiple applicators held in place by packing. A radiograph taken a few hours after the insertion of such applicators is usually very disillusioning if one is greatly concerned about accuracy.

(3) *Danger to personnel in handling:* Very few applicators at present in use have been so designed that all handling during loading and most of the manipulation in placing the applicator in position during treatment may be done by means of forceps.

Description of New Type Radium Applicator.—In an attempt to overcome some or all of these objections we have designed an applicator which we believe has certain advantages. It consists of two end-pieces in which the radium is loaded, which are separated from each other by a bridge or spacer. The end-pieces follow the design originally described by Paterson and Parker and conform to the shape of the field of intensity around any radium source. Originally, these were in the form of hollow shells of spun brass, chromium plated, and in the centre of each is a platinum-iridium tube of 0·5 mm. wall thickness. This tube may be made of any size of thickness to carry any radium loading which may be decided upon. A cover is provided which is so designed that in loading it can be raised and lowered entirely by instruments. The most recent model of this applicator is made of nylon which entirely eliminates all metal parts, is strong and rugged in use and may be sterilized by boiling. Nylon has a molecule composed of carbon, hydrogen and nitrogen, all elements having the same atomic numbers as tissue, and has the further advantage of being free from impurities of high atomic numbers such as frequently occur in rubber (i.e. sulphur, &c.).

The bridge or spacer is provided with apertures into which a "fork" is fitted during the manipulation of placing the applicator in position against the cervix. Once in place the applicator is locked and is under complete control of the operator and may be placed and held in any position desired. Light packing is inserted merely for the purpose of keeping the tissues out of contact with the instrument. The distal end of the controlling "fork" protrudes from the vaginal orifice and is fastened to a belt which the patient wears throughout the treatment. (A self-retaining catheter is inserted before the belt is finally adjusted, and suitable pads are used for protection.) (Shown in figs. 1, 2 and 3.)

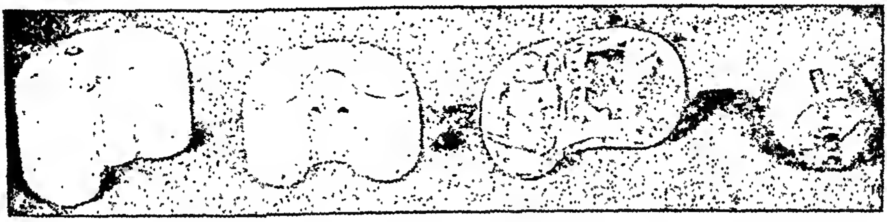


FIG. 1.—Photograph showing the four sizes of vaginal applicators described.

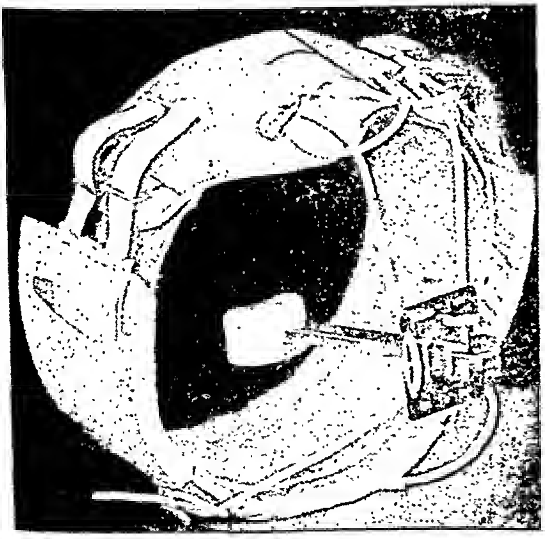


FIG. 2.—Applicator and belt as used, showing fork and method of fixation.

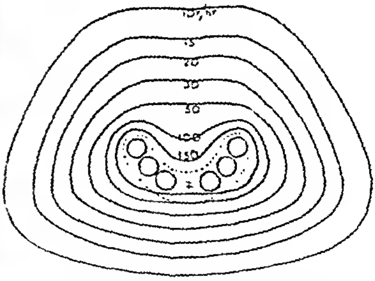


FIG. 3.—Curves showing distribution around the vaginal applicator described.

1–10 mg. tube with 1 mm. Pt filtration in each pocket. Total radium in applicator – 60 mg. Total filtration of each 10 mg. source – 1·5 mm. Pt.

Note the flattening of the intensity posteriorly, although in this case no added filter is used.

Once in place this applicator cannot slip from the position in which it is placed in any direction whatever, either towards either side or, perhaps even more important, cannot either tip over, facing the bladder and rectum (which is without doubt the most common cause of cystitis, proctitis and recto-vaginal complications), or be partially expelled. Four sizes of the applicator are available and provide amply for the requirements of individual selection and make provision for radium sources ranging from 10 mg. in each end of the applicator to as high as 90 mg. in each end. This could be increased (by altering the filter and making use of some of the new radio-active substances) up to ½ gramme of radium in each end of the applicator, if such a change in method can be shown to have any advantages.

Protection of the rectum.—In the past one of the most troublesome complications in the treatment of cervical carcinoma has been due to proctitis, either during or following the completion of therapy. Measurements made with conventional applicators show that in most cases in which adequate dosage has been delivered the dosage reaching the recto-vaginal septum has usually been above 5,000 r, which is about the tolerance limit of the rectal mucosa. In the applicator here described the rectum is protected by means of a special built-in filter. In the present applicator the material used for this filter is either gold, platinum or lead, but in the future and as soon as it becomes available metallic uranium will be used for this purpose, as suggested by Professor W. V. Mayneord. Owing to its very high atomic weight this metal is especially suitable for the purpose. By this means the intensity of radiation reaching the rectum can be reduced 25–30%, or even more if desired, thus permitting the use of as high dosages in the parametrium as these tissues will tolerate.

The intra-uterine applicator is a simple tandem in rubber tubing as, in our experience, this, by reason of its greater flexibility, tends to ease of insertion.

Dosage.—The dosage in each individual case is determined by a calculation (with apologies to all physicists) which takes into consideration the dose which has already been delivered by means of roentgen therapy.

If the plan of treatment has all been charted prior to the commencement of the roentgen series the dosage of radium required will be known and will be the amount required to build up the total to that which is lethal for cancer, or to the tolerance limit of the pelvic tissues.

Some indication as to the degree to which the individual tumour may be expected to respond will have been gained during the roentgen series, or at least prior to the administration of the radium, and this will influence the loading of the radium applicators as well as the total dose delivered. In an average case the intra-uterine tandem would carry 40 mg. enclosed in 1 mm. platinum filter, while the vaginal applicator already described would be loaded with 30 mg. in each end filtered by 1·5 mm. platinum. Under these conditions 3,500 mg.hrs. will be delivered in 87½ hours. Thus the decision to be made is whether this is sufficient or whether either the roentgen dose should be increased or that of the radium. Having reached this decision it would be modified in actual practice only in case the patient fails to tolerate the roentgen therapy well.

TABLE VI.—DOSAGE DELIVERED BY RADIUM THERAPY (IN ROENTGENS)

Type of applicator	No. of mg.hrs.	Point A	Point B	Point C	Point S
Intra-uterine tandem (40 mg.)	3,000	3,690r	780r	420r	250r
”	4,000	4,920	1,040	560	320
”	4,200	5,170	1,100	590	350
”	5,000	6,150	1,300	700	400
Intravaginal (2 × 30 mg.)	3,000	1,050	570	360	1,800
”	4,000	1,400	760	480	2,400
” . .	4,200	1,470	800	500	2,500
”	5,000	1,750	950	600	3,000

Final total dosage.—The final totals are added and recorded on a form, and while it is recognized that from the physicist's point of view there are objections to such additions, yet in practice the advantages are very great and permit a degree of dosage control not otherwise possible. In a busy department, with constantly changing personnel. such control is absolutely essential in order to reach and maintain a high technical standard and avoid serious injuries.

Intravaginal roentgen therapy.—Several writers, notably Merritt of Washington, have advocated the use of intravaginal roentgen therapy as a substitute for radium. Having tested this procedure out very thoroughly over the past six or eight years, we are convinced that although it has a useful place in the treatment of cervix carcinoma, it is not a "substitute" for radium. Merritt's most recent figures show a considerably lower five-year cure rate than may be obtained either by radium alone or by the combination of roentgen therapy and radium as described in this paper.

If our experience is an accurate guide it would indicate that the proper field for intravaginal roentgen therapy is in the advanced case with complete occlusion of the cervical canal or actual destruction of the cervix where the intracervical or intra-uterine application of radium will be impossible. Our present routine calls for this procedure in most Stage IV cases and selected cases in Stage III, where it is combined with external roentgen therapy and carried to a total vaginal dose of 3,000 r, using X-rays at 200 kV., filtration 0·2 mm. Sn., H.V.L. 1·9 mm.Cu. As will be evident from the statistics here reported the five-year survivals have not been improved to any very marked degree, although many cases have shown very gratifying degrees of healing by this method.

SUMMARY

(1) The results of treatment of cervix cancer by surgery and by radiotherapy have been compared. Radiotherapy is still producing substantially better five-year results and is applicable to a much higher percentage of the total cases.

(2) Results by radiotherapy in 1,261 cases here reviewed, of which 756 are over five years, were:

Net Survivals		Gross Survivals (no deductions)	
Stage I	80·0%	Stage I	71·25%
Stage II	53·66%	Stage II	48·78%
Stage III	31·83%	Stage III	29·06%
Stage IV	9·22%	Stage IV	6·38%
Average for all cases	39·8% 5 years 29·1% 10 years	Average for all cases	35·71% 5 years 21·9% 10 years

(3) The evidence indicates that definite progress has been made during the past ten years and means are available by which further improvement should be achieved in the future. Some suggestions by which this may be brought about are offered.

(4) A new type radium applicator is described which appears to have certain advantages in the technical application of radium to the cervix.

REFERENCES

1 Meigs, J. V. (1944) *New England J. Med.*, 230, 577; (1945) *Amer. J. Obstet. Gynec.*, 49, 542.

2 Paterson, R., Tod, M., and Russell, M. (1946) Result of Radium and X-ray Therapy in Malignant Disease, Second Statistical Report from the Holt Radium Institute, Manchester, 1934–38. Edinburgh.

This paper includes quotations from an article on the same subject, accepted for publication by the *American Journal of Roentgenology*, to which acknowledgment is made.

Mr. G. W. Blomfield, (*Medical Director, Sheffield Radium Centre*): In the treatment of carcinoma of the cervix uteri the average figures for five-year cures of all cases seen in large centres range around 25% for radiotherapy, and for surgery it is less. The failures and the complications from radiotherapy result mainly from: (1) Recurrence or persistence of growth. (2) Radiation damage.

Recurrence.—A true recurrence may take place in a precancerous lesion which may persist after the growth is cured. Most "recurrences" are examples of persistence of growth. The site of the recurrence may be local or distal.

Local "recurrence" almost invariably occurs if patients default treatment after receiving only one-third or one-half of the planned therapy. If full dosage is given local cure may result, provided local spread is not too extensive, in which case it is, of course, difficult to get a homogeneous dosage high enough to be lethal to the primary growth.

Distal "recurrences" are likely to occur whenever there are distal metastases or metastases outside the area treated to high dosage. Remote "recurrences" are at present avoidable only by getting patients under treatment before remote metastases arise.

Anatomically the problem is different for different stages of growth. The Stage I case with growth limited to the cervix is a comparatively simple problem. Provided the whole of the cervix is treated adequately, and the cervix will certainly take a very high radiotherapeutic dose, a cure should result. It is the Stage II and Stage III cases which present the difficult problems and Stage IV cases which present problems at present insuperable.

Briefly, the treatment problem resolves itself into the following parts: (*a*) What to treat. (*b*) What doses should be given to these areas. (*c*) By what technique we may best achieve these dosages to these areas.

Factors such as dosage rate, fractionation and overall time all have a bearing on biological effect.

In the more advanced stages of the disease there is usually an irregular area involved from the cervix into the parametrium and over the vaginal vault, and the dosage of all areas likely to be involved is liable to be insufficient by ordinary techniques without exceeding tolerance dosage in some important adjacent organ such as bladder, bowel or ureter.

The reasons for these insufficiencies are as follows: (*a*) It is difficult to assess the exact spread of the growth. (*b*) The possible areas affected are in close relation to important structures such as rectum, bladder and ureters and dosage to these structures must be safe. (*c*) Anatomical variations and the alterations consequent upon disease make standard distribution of radium and constancy of dosage impossible.

Possible Sites of Damage

Vaginal mucosa.—The vagina tolerates very high dosage itself. Ordinary techniques commonly used give 15,000 r locally without causing much more than adhesions and contractions. High dosage associated with sepsis or with damage to bowel or bladder is dangerous.

Rectum.—This is exposed to danger in two places: (1) High up—near pelvi-rectal junction, where it may be in close relation to the pouch of Douglas or cervix. (2) In its relation to the posterior vaginal wall.

Bladder.—This is exposed to maximal dosage at the base and may undergo late necrosis with fistula formation. More commonly a telangiectasis arises visible on cystoscopy, usually harmless, but sometimes causing recurrent hæmaturia.

Ureters.—These are further out than commonly supposed. They are about 3 cm. from the mid-line and approximately 1 cm. lateral to the point A (defined below), as they pass the cervix to sweep forwards and inwards towards the trigone. They are seldom damaged by the irradiation itself and rather by growth or fibrosis and sepsis than by radio-necrosis.

Small intestine and pelvic colon.—These viscera come in close relation to the fundus uteri, the posterior uterine wall and occasionally to the pouch of Douglas and cervix uteri, with consequent high dosage at times.

Bearing in mind possible damage to these areas cases have been collected at Sheffield for data regarding the incidence of consequent complications, and then dosage was assessed in roentgen units at the sites where damage was known to occur.

Using three treatments over two or three weeks the safe tolerance doses would appear to be in accordance with the following table:

Structure	Tolerance locally in roentgens
Rectum	4,000
Base of bladder	5,000
Bowel in contact with posterior uterine wall or fundus	5,000
Vaginal vault	12,000 to 15,000

Careful analysis of the cases for dosage where radiation damage resulted showed that these tolerances had been exceeded in such cases. Damage attributable to radiation did not occur otherwise.

Physical problem.—Once the ideal dose distribution has been decided on clinical and biological lines, it is then possible to work on the technique with a view to obtaining this. The classical Stockholm and Paris techniques each represent such an attempt. The Manchester technique [1] is a modification of the Paris one, using different timing and modified colpostats, and the dosage system adopted there aims at giving a fixed limit to the point A in the pelvis, defined in position as 2 cm. lateral to the mid-cervical line and 2 cm. above the vaginal vault. The point B at the same level and 5 cm. from the mid-line is taken as an outlying point to which as high a dose as possible should be given without exceeding the fixed limit at A. Neary [2] in 1943, showed that the system of pushing the radium as far out laterally as possible did not necessarily give the highest ratio of dosage B to A. Additional screenage of one sort or another has been employed on and off since the early days when bismuth packing was tried. In 1944 I used a lead applicator with two radon sources placed centrally. By this means it was possible to give relatively large dosage as measured in milligramme hours without causing rectal damage, the lead being mostly situated between the radon sources and the rectum. Neary has designed a two-source platinum applicator to which the uterine radium can be fixed in position and this delivers a fairly constant dose across the pelvis. It has been tried clinically by Mr. Malcolm Donaldson.

Single-source vaginal applicator.—This is a single vaginal source placed centrally in the mid-line and shielded by platinum to diminish dosage to bladder, rectum and the pouch of Douglas. The first applicator designed consisted of a central sphere of platinum, 3 cm. in diameter, hollowed out so that there was 1 cm. screenage of the rectum and ½ cm. screenage of the bladder, the radium being placed centrally. Ports cut through the sphere allowed free radiation to the fornices and out to the parametria on each side. At Mr. Donaldson's suggestion the radium was loaded on the end of a rod to be inserted after positioning of the applicator. The applicator is held in position by a handle and special belt fixed to the patient. Perspex spaces of different sizes are used to pack off the vaginal wall and diminish the dosage immediately over the ports where screenage is minimal, and this takes the place of the packing ordinarily used with standard techniques. The shielding of the pouch of Douglas was found to be important in the earlier work using two radon sources and this was arranged for. The ideal direction for the beams issuing through the ports was determined by taking a number of measurements on cadavers, to determine the direction from the radium source at the centre of the sphere to the parametrium and adjacent pelvic wall so as to include likely extensions of growth.

A second and more versatile appliance was designed later to give the same essential protection to the rectum and bladder but allow movement of the sphere which could be rotated through 45 degrees in the sagittal plane to enable adjustment of the beams to meet varying clinical requirements. It also allowed for replacement of platinum screenage in the direction of the cervix by brass or aluminium, a detachable cap being used. This enabled good dosage to be delivered to the cervix and uterus when no uterine radium could be inserted and it has proved of great value, the 45 degree adjustment enabling the cervix and uterus to be effectively irradiated in these cases even when there is anteversion or retroversion.

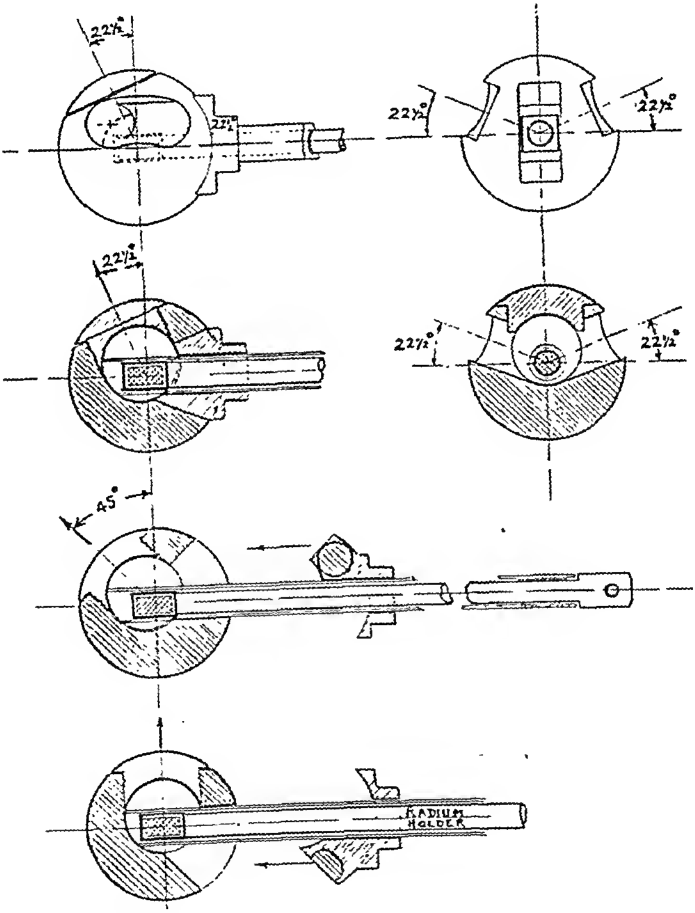


Fig. 1 illustrates the mechanism of the applicator in elevation and cross section. The radium, when inserted, lies in the centre of the sphere and the lateral beams are directed slightly upwards and backwards as shown. The platinum cap when replaced by aluminium permits the use of a vertical beam which can be rotated through 45 degrees in the sagittal plane and directed to the uterus, as shown in the diagram.

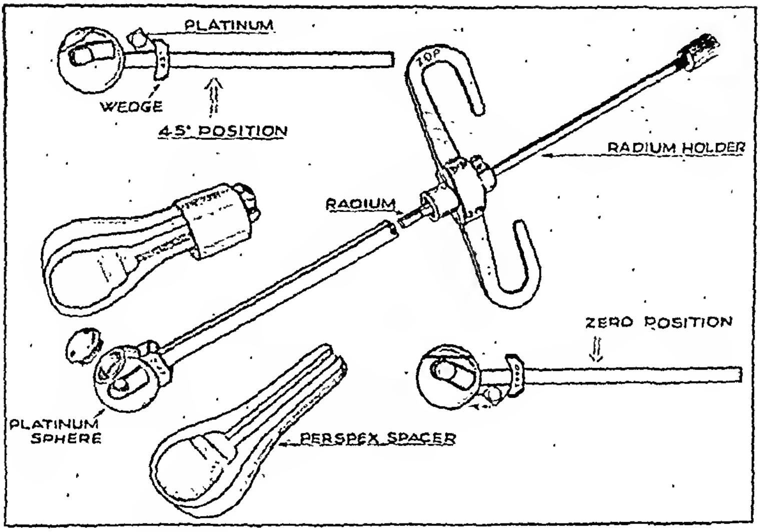

PLATINUM
WEDGE
45° POSITION
TOP
RADIUM HOLDER
RADIUM
ZERO POSITION
PLATINUM SPHERE
PERSPEX SPACER

Fig. 2 illustrates how the applicator is assembled. The spacers shown can be of different sizes, the largest size which can be easily inserted is used, and the treatment time should be adjusted to give approximately uniform dosage on the outer surface. The wedges fix the sphere in position and allow adjustment of the beams. The instrument is precision made and will only assemble with the handle the right way up so as to ensure correct alignment. When the radium holder is screwed home the radium is exactly central.

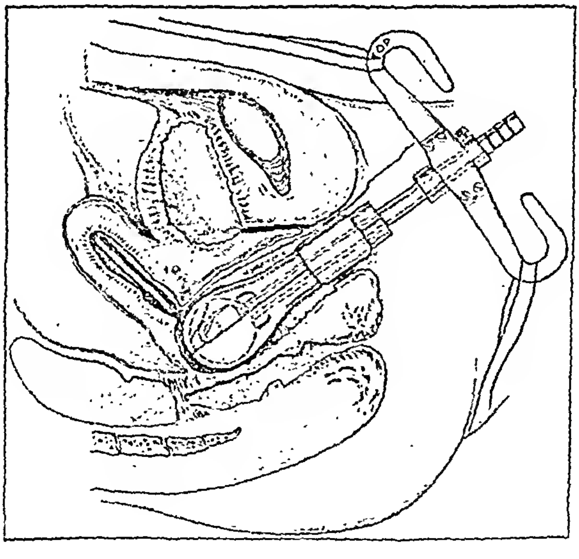


Fig. 3 shows the applicator and uterine radium in position and the anatomical relationships as viewed in sagittal section.

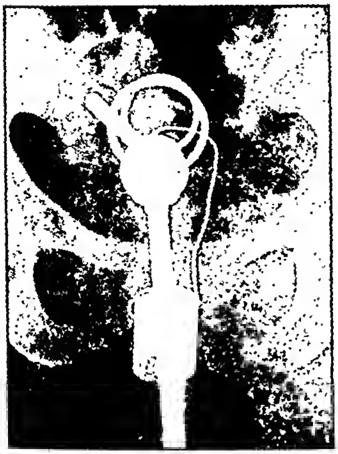


FIG. 4.

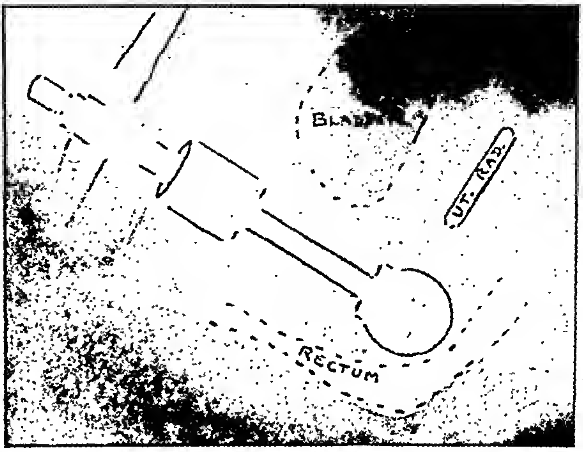


FIG. 5.

Figs. 4 and 5 show radiographs of the applicator in position. In fig. 5 the rectum has been injected with opaque medium and the bladder with air; the rectum showing in white and the bladder as a dark shadow. In fig. 4 the rings are outside the patient and are there to facilitate accurate analysis of stereoscopic radiographs.

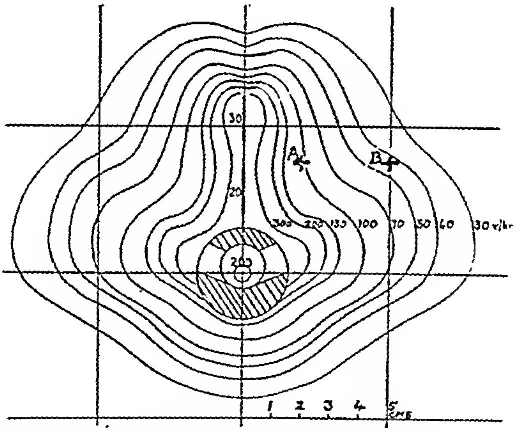


Fig. 6 shows isodose curves calculated for the applicator in conjunction with a 50 mg. uterine source, and illustrates well the slow falling off in radiation towards the parametrium and pelvic wall. Point A shown on the diagram is 2 cm. above the vaginal vault and 2 cm. lateral to the mid-line of the uterus. Point B is on the same level but 5 cm. out from the centre of the uterus towards the pelvic wall. Full physical data showing isodose curves for comparison with other techniques would require numerous illustrations. These and other details can be supplied on request.

The dosage system at present adopted aims at keeping within tolerance to vagina, bladder, rectum, pouch of Douglas and uterine surface, and generally speaking this allows vaginal radiation to 10,000 mg.hrs. using a 200 mg. source of pure radium in addition to uterine radiation of approximately 2,400 mg.hrs. Graphic methods are used for the rapid calculation of dosages to rectum, bladder and other important structures. The vaginal radium can be inserted and removed without disturbing the appliance or moving the patient but the actual dosage given should depend upon the size of the spacers used and the relative position of uterine radium and vaginal applicator as shown on the antero-posterior and lateral radiographs taken with vaginal radium out to avoid fogging.

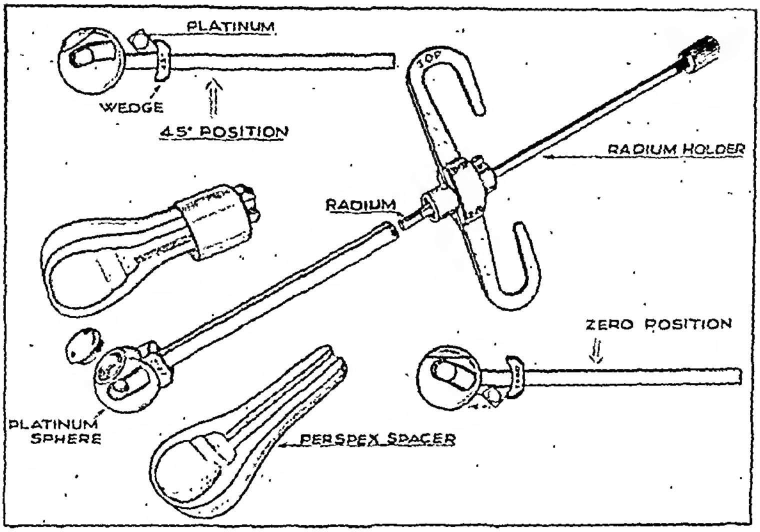

PLATINUM
WEDGE
45° POSITION
TOP
RADIUM HOLDER
RADIUM
ZERO POSITION
PLATINUM SPHERE
PERSPEX SPACER

Fig. 2 illustrates how the applicator is assembled. The spacers shown can be of different sizes, the largest size which can be easily inserted is used, and the treatment time should be adjusted to give approximately uniform dosage on the outer surface. The wedges fix the sphere in position and allow adjustment of the beams. The instrument is precision made and will only assemble with the handle the right way up so as to ensure correct alignment. When the radium holder is screwed home the radium is exactly central.

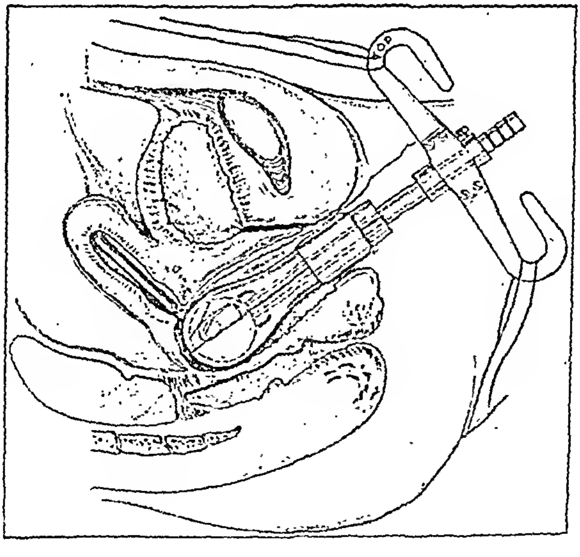


Fig. 3 shows the applicator and uterine radium in position and the anatomical relationships as viewed in sagittal section.

Section of Epidemiology and State Medicine

President—W. S. C. COPEMAN, O.B.E., F.R.C.P.

[*October* 6, 1947]

DISCUSSION ON ANTERIOR POLIOMYELITIS

Mr. K. I. Nissen: *Poliomyelitis on St. Helena*, 1945-6.

Towards the end of 1945, the remote community on St. Helena suffered a severe outbreak of poliomyelitis, a disease unknown on the island within the memory of its oldest inhabitants. In 1836, however, Sir Charles Bell mentioned an epidemic fever among the young children on St. Helena, followed in all cases by "a want of growth in some part of their body or limbs". This may be the earliest reference to epidemic infantile paralysis in the English literature [1].

The following brief account of the epidemiological features of the recent outbreak is given with the kind permission of Dr. Wilson Rae of the Colonial Medical Service. In October 1945 I had spent a few hours on the island *en route* from South Africa by transport. When the epidemic was at its height, Dr. Rae, on Professor H. J. Seddon's suggestion, secured my immediate release from naval service and a quick return to St. Helena for a stay of six weeks.

THE ISLAND AND ITS POPULATION.—St. Helena is situated in the South Atlantic Ocean roughly 16° South and 6° West (*see* Map). It has an area of 47 square miles and is of volcanic formation. The principal feature is a semicircular ridge of mountains rising to 2,700 feet, part of the weathered rim of a great crater. From this ridge steep valleys stretch in all directions; many contain small streams, and springs of good water are abundant. The island is everywhere mountainous, the sea-face being generally formed by cliffs several hundred feet in height. The only practicable landing place is on the leeward side from an open roadstead at St. James' Bay, where in normal times one Union Castle vessel anchors each month.

Climate, vegetation and supplies.—The climate is healthy and temperate owing to the constant south-east trade wind. The rainfall reaches 40 inches in the hills, but on the lower slopes it is derived from light drizzles and is of little value.

The coastal zone is mainly rocky and barren except for prickly pears. The middle zone is partly under grass, with some small areas under afforestation. The central zone is largely under flax, which affords the main industry. Agriculture is on a small scale, with less than 5 acres under irrigation. All grain and flour are imported. The main foodstuffs of local origin are potatoes, bananas, yams, fresh vegetables and plums. During the war there was rationing of meat, rice, fats, sugar and latterly flour. The small fishing industry provides an important source of protein mainly from the albacore or tunny, but catches are variable and distribution is uneven. Half the small supply of cow's milk is consumed by Europeans. Bread, potatoes and fish are the staple articles of diet among the islanders, with sweet tea as a beverage.

The population.—A recent estimate was 4,000. Of these the British in the garrison numbered less than 200, with a similar number in Government service and commerce. The remainder, here called "islanders", are of mixed extraction, mainly from the East Indies, West Africa and Great Britain. In peacetime there is a steady exodus to domestic service and industry in South Africa, while recruiting into the British Army abroad has begun. The proportion of children therefore tends to be high.

The wartime garrison, housed in barracks at the top of Ladder Hill, included about 70 island recruits. Local enlistment ceased in the middle of 1944, and a number of men had returned to civilian work on the island.

Towns, roads and housing.—The capital, Jamestown, is situated at sea-level in the length of a narrow valley, and has 1,500 inhabitants in its crowded houses. Apart from villages at Half-tree Hollow, Longwood, and round the cable station at The Briars, the island homes are widely scattered. The

This form of applicator has now been in use for sufficient time to assess its clinical possibilities and used on these lines it is safe. It gives known dosage which can be accurately calculated, and it presents the advantages mentioned, including the possibility of giving effective cervical dosage when uterine radium cannot be inserted. It appears likely that this form of technique or something similar using heavy metal screenage will eventually replace the more classical techniques employing boxes, colpostats or pessaries.

For the clinical trials 200 mg. beam unit tubes were used for convenience. It is now proposed to use a 125 mg. vaginal source for routine work in conjunction with uterine sources of 20 mg. in the upper uterine tube, and 10 mg. in the lower uterine tube for the average-sized uterus. The treatment is given in two applications.

My thanks are due to Dr. H. Miller, M.A., Ph. D., F.Inst.P., Senior Physicist to the Sheffield National Centre for Radiotherapy, for his invaluable help and his patience in calculating and measuring isodose surfaces, and to Messrs. Johnson Matthey & Co. Ltd., who manufactured these applicators, for which they have had to make special jigs and templates. I am also indebted to the Medical Research Council for meeting the cost of the applicators and to the National Radium Commission and the National Radium Trust for the radon and the pure radium, without which this work could not have been carried out.

REFERENCES

1 TOD, M. C., and MEREDITH, W. J. (1938) *Brit. J. Radiol.*, **11**, 809.
2 NEARY, G. J. (1943) *Brit. J. Radiol.*, **16**, 225.

Mr. Frank Cock (*London*): Every case of carcinoma of the cervix should be treated by a combination of methods. Each case should be assessed in accordance with its merits and with the local and general condition of the individual patient.

With regard to surgical treatment, I do hope Mr. Read has proved to your satisfaction that the danger to life of Wertheim's operation has been grossly over-stated. The post-operative mortality in skilled hands and in selected cases, with modern accessories, should be inconsiderable.

I have long been convinced that, pending future discoveries and developments, the best treatment for carcinoma of the cervix consists of (*a*) radical hysterectomy plus deep X-ray therapy or of (*b*) radium plus deep X-ray therapy, in accordance with the features of the individual case. (I cannot see the point of combining the vaginal and intra-uterine application of *radium* with radical hysterectomy, as it seems to me that they cover more or less the same field.) In the former group I suggest that a preliminary course of deep X-ray therapy should be followed by a radical hysterectomy ten days or a fortnight later. The operation should be followed by a full course or courses of deep X-ray therapy as soon as the patient is fit to undergo such treatment. This implies that surgical and radiological facilities ought to be available in the same institution or in immediately adjacent hospitals. The patient must not have to wait in a queue for admission from one hospital to another at a distance. My second main group, involving a combination of radium and X-ray therapy, I leave of course to the expert radio-therapists. This group consists, in my view, of cases that are inoperable, and possibly of some *very* early cases.

I have been most highly impressed by Professor Subodh Mitra's exposition, by his amazing dexterity, by his honesty of statement and by his good results. But I do submit that it is impossible to extirpate by the vaginal route the obturator glands and those glands which are so closely attached to the great iliac veins. Those of us who perform Wertheim's operation are well aware how frequently these glands are affected.

In radio-therapeutic technique the excellence of the results of Dr. Gordon Richards and Dr. Blomfield, and their promise of still further progress in this direction, are most encouraging and inspiring.

Let us beware of too much de-centralization in future planning. The essence of the whole matter lies in co-operation. Sooner or later it is inevitable that large radio-therapy centres will be established in the various regions—possibly at a considerable distance from the main centres of population and from the large general and gynæcological hospitals. One cannot but feel that the surgeon, and perhaps even clinicians in general, will play a very subsidiary part in these highly specialized institutions. I do therefore recommend most strongly that *every* form of relevant therapy should be represented at or very near to the general or gynæcological hospital, where the exponents of each and every method may confer and combine in the treatment of all cases of cancer before these cases are finally transferred. I would further dare to suggest that a clinician, not necessarily a surgeon, should control the situation throughout: we are treating a patient, not merely a neoplasm.

who developed symptoms thirty-one days later and died. This young woman continued on friendly terms with members of the garrison after his visit of some two hours.

The transport embarked a mixed contingent of British and St. Helena troops. Among the former was an artillery sergeant who reached his family in Ealing on October 29. Eleven days later his daughter developed severe poliomyelitis and when admitted to Clayponds Isolation Hospital was the first patient from the district for over a year. The father could not recall any personal illness like an abortive attack.

It is unlikely that the garrison provided the source of infection. Just before and during the epidemic the garrison was free from cases of obscure pyrexia, and in any case ample opportunity for any transmission of infection had occurred since the last overseas reinforcements three months previously.

It does appear significant that the first case, a fulminating one, was visited by a person less than a week out from South Africa, an endemic area. Though the suggested incubation period of thirty-one days is remarkably long, it is still less than the thirty-five days considered to be the upper limit by American workers [2]. In crowded Jamestown, however, the visit mentioned could not be regarded as an "only possible exposure". The Ealing infection was also compatible with the presence of carriers on board the transport.

Spread of the epidemic (Table I).—After the first death a few apparently trivial cases of illness were not recognized at first as poliomyelitis. A boy of 5 with fever and generalized spasm and twitchings was thought to be suffering from the common Ascaris infection, but developed a temporary facial palsy. A boy of 10 had obscure pain in the left axilla, and the lower half of the pectoral muscle was later found paralysed. A labourer, the only case admitted to hospital with a diagnosis of influenza, had paresis of the deltoids which was not recorded for a few days. But on November 29, eleven days after the first death, a second patient gravely ill was admitted and died on December 1, a day on which a number of obvious cases reported. The first phase, lasting a fortnight, was now over. The epidemic reached a peak in the next two weeks, and then subsided to spend itself gradually over a period of six weeks. I arrived by H.M.S. *Shiel* from Capetown on December 23 and sailed again on February 1.

TABLE I.—TO SHOW INCIDENCE OF CASES BY WEEKS

		Nov.		Dec. 1945				Jan. 1946					Feb.
Week ending		21	28	5	12	19	26	2	9	16	23	30	6
Fatal ..	(11)	1	1	4	2	1	1	0	1	0	0	0	0
Paralytic	(66)	3	6	22	14	7	6	2	1	2	2	0	1
Abortive	(140)	0	3	48	52	14	9	6	2	3	2	1	0
Totals	(217)	4	10	74	68	22	16	8	4	5	4	1	1

The epidemic list in order of onset showed intervals of nine and twelve days between the first Jamestown case and the first cases in the neighbouring areas of Half Tree Hollow and The Briars. The intervals for first infections in the distant Longwood and Sandy Bay areas were thirteen and seventeen days. Graphs for the three main districts showed a marked time lag in the Sandy Bay area, from whence came, as expected, the majority of late cases.

Method of spread.—The living traffic between Jamestown and the outlying districts is almost confined to adults and donkeys. There are long stretches of barren road, so that flies and rats are unlikely vectors. The only fresh foodstuffs distributed to the periphery are bread and fish. The latter may be carried exposed for long distances, but the epidemic lacked the explosive character associated with contamination of food. Water supplies are from numerous fresh sources. Milk is brought always into Jamestown. There was in fact no evidence to conflict with the opinion that the spread was commonly by contact with adult carriers.

CLINICAL FEATURES.—The symptoms and course of the illness were fairly typical and it is not proposed to make detailed comments. There were two noteworthy signs however.

The colour of the tongue was noticed to be characteristic by Dr. Lee and his colleagues early in the epidemic. Despite the pyrexia the tongue was moist and not furred. Its general

60 miles of roads passable to motor traffic are mainly steep and stony. Traffic goes mostly by foot or donkey, and to a small extent by motor vehicle.

The typical island house consists of a row of two to four small rooms, each with an outside door. The walls are of stone with mud plaster and the woodwork suffers badly from the ravages of ants. Overcrowding is common and frequently gross. A Government building scheme is in progress but has not advanced enough to affect the acute shortage of houses. Water is obtained by hand from the nearest water tank or spring. Night-soil is collected in buckets, but the stony ground makes disposal difficult. Conditions in Jamestown, however, are much better with regard to water supply and drainage. The common pests are the house-fly and the rat. Domestic gardens are either absent or small.

Conditions preceding the epidemic.—The conditions on the island at the time of the epidemic were unusual. Drought was affecting all areas, with failure of the potato and vegetable crops. Low stocks of flour had made strict bread rationing necessary. There was clinical evidence of vitamin-B deficiency and little doubt that the average intake of vitamin C was below normal. A small epidemic of anthrax in cattle had subsided, though recently enough for many islanders to use the same word for cases of poliomyelitis.

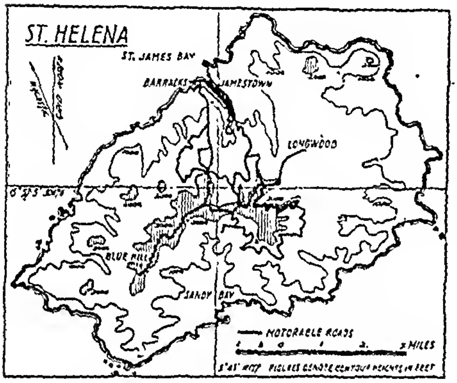


FIG. 1.—Contour map of St. Helena, showing geographical features and main roads in heavy lines.

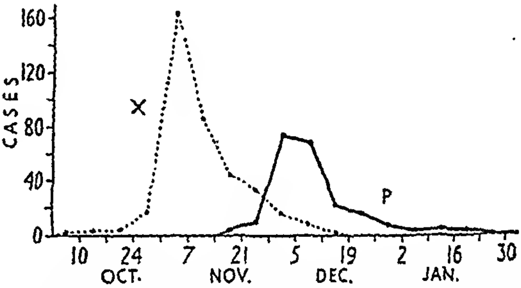


FIG. 2.—Graph to show incidence by weeks of "Influenza" (X) and of Poliomyelitis (P), abortive cases included.

Two weeks previous to the first case what was regarded as the annual outbreak of influenza had reached a very high peak (*see* Graph). Most of the 385 cases had fever with headache, general aches and pains and a sense of weakness in the limbs; only one was admitted to hospital with this diagnosis. The outbreak had not subsided when the epidemic began, and it is probable that there were some cases of cross diagnosis between "influenza" and abortive cases of poliomyelitis. Apart from the single case mentioned above, no case labelled influenza attended later with a specific muscular paralysis. This and the interval of three weeks between the peaks of the two infections suggest that the earlier outbreak was not a carrier wave, though it may in some way have prepared the ground for the coming epidemic.

THE COURSE OF THE EPIDEMIC.—On the evening of November 14, 1945, the first patient, a woman of 25, was taken ill in Jamestown with malaise and vomiting. This continued the next day, but the added fever, headache, backache, irritability and drowsiness were thought to be no more than symptoms of influenza. When seen first by a medical officer on the 16th, signs at the right base and a respiratory rate of 40 led to a provisional diagnosis of pneumonia with septicæmia. Typical paralysis of the legs and respiration developed, however, and the correct diagnosis was made before death.

Possible sources of infection.—To anticipate, there is no doubt that the strain of virus was one to which the islanders were highly susceptible and the European population almost immune. The last ship to call before the onset of the first case was H.M.T. *Reina del Pacifico* bound for Liverpool from Durban and Capetown with 2,800 persons on board. The passengers were mainly Service personnel, together with 350 women and children, for whose medical care I was chiefly responsible. Poliomyelitis was common in South Africa at this time. Apart from a few cases of measles the voyage was uneventful and no fresh invalids were transferred to hospital at Liverpool on October 28.

The transport lay off Jamestown on October 14. Several small parties of officers went ashore, myself included, but only one of the other ranks, a corporal who had previously been stationed in St. Helena. He obtained permission to visit his fiancée, the first patient, *Incubation periods.*—A few cases of value from this aspect occurred early in the epidemic.

(*a*) Short and (?) only possible exposure. The long period of thirty-one days for the first case has already been discussed.

(*b*) Maximum exposure. The Ealing case developed after eleven days. A patient and a clerk in the Civil Hospital developed severe infections twelve and eighteen days respectively after the admission of the first case.

(*c*) Minimum exposure. The second fatal case developed after the whole family had been isolated for four days.

METHODS OF CONTROL.—As soon as succeeding cases of obvious poliomyelitis were diagnosed, the disease was made notifiable, hospital treatment was made free, and measures restricting congregations of people were adopted. The schools being already closed from "influenza", church services and cinemas were discontinued, and gatherings of more than four persons, whether in shops, public houses or vehicles, were forbidden. The garrison was confined to barracks, a measure which many of the soldiers had already adopted. A review of the restrictions suggests that in view of the probable high susceptibility of the islanders, the stern warning of the first fatal case would have justified immediate action. All restrictions were lifted on January 26, by which time the epidemic had subsided. Certificates of fitness were required of all children returning to school, and this gave an opportunity to detect unreported cases of paralysis.

SUMMARY

The St. Helena epidemic of poliomyelitis affected a virgin island population. It commenced in Jamestown in November 1945 and after some delay spread to the outlying districts. There was some evidence that the virus was introduced from South Africa, an endemic area. The incubation period of the first case may have been thirty-one days. The highest incidence occurred in the three age-groups between 5 and 19. Abortive cases numbered two-thirds of the total and, when included, gave an all-over rate of recorded infection of 5·4%. Seventy-seven cases were paralysed, giving an attack rate of 19·2 per thousand. Eleven fatal cases gave a death-rate of 14·3% of all paralytic cases.

REFERENCES

1 BELL, C. (1836) The Nervous System of the Human Body. Edinburgh, 434-5.
2 CASEY, A. E. (1942) *J. Amer. med. Assoc.*, 120, 805.
3 AGIUS, T., BARTOLO, A. E., COLEIRO, C., and SEDDON, H. J. (1945) *Brit. med. J.* (i), 759.

Dr. L. J. Maurice Laurent: *Acute meningo-encephalitis of undetermined virus ætiology.*—During a short period of seven weeks in the summer of 1946, 13 cases of an acute infection of the nervous system of an unusual type were admitted to the Park Hospital with the diagnosis of cerebrospinal fever. Judging from the clinical picture and the pathological findings, they were apparently instances of one and the same disease. All but one recovered, the fatal case died in coma on the sixth day of the illness.

History of sudden onset with headache and fever. The symptoms became worse during the next few days and admission to hospital occurred usually between the fourth and sixth days. *On admission*, the clinical signs of meningitis were evident in all. 7 were alert, 4 listless or drowsy and 2 unconscious. No rash of any kind. *Cranial nerves:* Fundi and ears normal in all. There was strabismus in 2, nystagmus in 2, transient deafness in 1, facial paralysis of supranuclear type in 6. *Plantar reflexes* flexor in 6, unilateral extensor in 5, bilateral extensor in 2. *Tendon-jerks*: Lost in 2, otherwise normal or exaggerated. Never any weakness or flaccid paralysis of any muscles of trunk or extremities on admission and afterwards. All abnormal neurological signs disappeared in fourteen days or less. No sequelæ have been observed. Pyrexial course variable, from six to twelve days.

Pathological findings and investigations.—Cerebrospinal fluid: clear or faintly opalescent, often with a fine clot on standing. Cells 40 to 800, 80 to 100% mononuclears. Protein 60 to 160 mg%. Chlorides always normal. Always bacteriologically sterile. X-rays of chest and nasal sinuses and also serum and blood tests revealed nothing abnormal. Specimens of the cerebrospinal fluid from 9 patients were examined by Dr. Findlay by animal inoculation and culture for the presence of a virus and all results were negative. Specimens colour was a cold bluish-grey, the shade obtained by pouring milk into blackcurrant juice. But round the margins small macules like flea-bites appeared and sometimes became confluent. These findings persisted for some two weeks, and were constant in all cases with paralysis. During the course of the epidemic very few "positive tongues" were seen in persons with no symptoms of infection. But at Longwood on January 29, Dr. Duncan examined 49 school children, all of whom were house contacts, and found that 27 had the type of tongue described.

The odour of the fæces was also characteristic. Several patients volunteered that the odour was offensive, like rotting vegetables, or like flax waste. The nursing staff in particular noticed the change from normal as many patients required enemata. The odour was independent of consistency and persisted for several days after the fall in temperature.

Age, sex and race (Table II).—Reference to Table II shows the very low incidence in children up to 5 years. No case was detected under one year, and there was only one case of severe paralysis in the whole of the first five-year period. The brunt of the infection fell on the three next five-year periods, with most deaths in the 15-19 age-group.

TABLE II.—TO SHOW AGE-INCIDENCE BY FIVE-YEAR PERIODS, AND SEX INCIDENCE

Age-Groups		0–4	–9	–14	–19	–24	–29	–34	–39	–44	–49	M.	F.
Fatal	(11)	0	1	2	5	0	2	0	1	0	0	3	8
Paralytic	(66)	5	19	13	15	8	2	1	3	0	0	38	28
Abortive	(140)	16	33	34	31	12	6	4	3	0	1	60	80
Totals	(217)	21	53	49	51	20	10	5	7	0	1	101	116

A striking contrast is afforded with the civilian epidemic in Malta, when 397 cases of paralysis occurred under 5 years and only 29 above that age [3]. Corresponding figures here are 5 and 61.

The only European patient was a girl of 10 living at the cable station who had an abortive infection. All others were islanders.

Abortive cases.—Abortive cases were numerous and well defined clinically. The epidemic list totalled 217. This included 11 deaths and 66 cases of paralysis. The remainder, 140, or roughly two-thirds of the total number, were cases with the criteria of infection but no definite paralysis. Many showed general weakness and inability to sit up for two or three days. Those cases admitted to hospital were quite indistinguishable from pre-paralytic cases. Two typical patients had lumbar puncture performed and cell counts of the order of 20 and 70 were found.

By no means all the abortive cases reported, as a number were treated in their homes with island remedies. The current out-patient organization, however, kept down the number of patients so missed. Cases presenting insufficient criteria to warrant inclusion in the epidemic list were fairly numerous.

The profusion of abortive cases became a serious problem. Thus an expectant mother, thought to have a mild infection, was sent home where she died. On the other hand many patients who proved abortive had to be admitted, especially from outlying districts, and retained in the crowded Civil Hospital till the risk of paralysis was over.

Deaths.—Fatal cases numbered 11, i.e. 14·3% of the total paralytic cases. The average time of death from the onset was 4·3 days, with limits of one and eight days.

Paralytic cases.—These totalled 66. With fatal cases included, the attack rate for paralysis was the high one of 19·2 per 1,000. By January 31, 28 cases remained paralysed and requiring orthopædic attention. The distribution of paralysis was a common one, with arms affected rather more than trunk muscles, and paralysis in the legs exceeding the total of other regions. Unilateral facial paralysis was observed in 5 cases, but was either transient or partial.

An estimate of the final extent of paralysis is as follows, counting severe paralysis of one limb or of the trunk muscles as a unit:—

3 to 4 units—2 cases; 2 to 3 units—6 cases; 1 to 2 units—5 cases; less than 1 unit—15 cases.

Incubation periods.—A few cases of value from this aspect occurred early in the epidemic.

(*a*) Short and (?) only possible exposure. The long period of thirty-one days for the first case has already been discussed.

(*b*) Maximum exposure. The Ealing case developed after eleven days. A patient and a clerk in the Civil Hospital developed severe infections twelve and eighteen days respectively after the admission of the first case.

(*c*) Minimum exposure. The second fatal case developed after the whole family had been isolated for four days.

METHODS OF CONTROL.—As soon as succeeding cases of obvious poliomyelitis were diagnosed, the disease was made notifiable, hospital treatment was made free, and measures restricting congregations of people were adopted. The schools being already closed from "influenza", church services and cinemas were discontinued, and gatherings of more than four persons, whether in shops, public houses or vehicles, were forbidden. The garrison was confined to barracks, a measure which many of the soldiers had already adopted. A review of the restrictions suggests that in view of the probable high susceptibility of the islanders, the stern warning of the first fatal case would have justified immediate action. All restrictions were lifted on January 26, by which time the epidemic had subsided. Certificates of fitness were required of all children returning to school, and this gave an opportunity to detect unreported cases of paralysis.

SUMMARY

The St. Helena epidemic of poliomyelitis affected a virgin island population. It commenced in Jamestown in November 1945 and after some delay spread to the outlying districts. There was some evidence that the virus was introduced from South Africa, an endemic area. The incubation period of the first case may have been thirty-one days. The highest incidence occurred in the three age-groups between 5 and 19. Abortive cases numbered two-thirds of the total and, when included, gave an all-over rate of recorded infection of 5·4%. Seventy-seven cases were paralysed, giving an attack rate of 19·2 per thousand. Eleven fatal cases gave a death-rate of 14·3% of all paralytic cases.

REFERENCES

1 BELL, C. (1836) The Nervous System of the Human Body. Edinburgh, 434-5.
2 CASEY, A. E. (1942) *J. Amer. med. Assoc.*, 120, 805.
3 AGIUS, T., BARTOLO, A. E., COLEIRO, C., and SEDDON, H. J. (1945) *Brit. med. J.* (i), 759.

Dr. L. J. Maurice Laurent: *Acute meningo-encephalitis of undetermined virus ætiology.*—During a short period of seven weeks in the summer of 1946, 13 cases of an acute infection of the nervous system of an unusual type were admitted to the Park Hospital with the diagnosis of cerebrospinal fever. Judging from the clinical picture and the pathological findings, they were apparently instances of one and the same disease. All but one recovered, the fatal case died in coma on the sixth day of the illness.

History of sudden onset with headache and fever. The symptoms became worse during the next few days and admission to hospital occurred usually between the fourth and sixth days. *On admission,* the clinical signs of meningitis were evident in all. 7 were alert, 4 listless or drowsy and 2 unconscious. No rash of any kind. *Cranial nerves*: Fundi and ears normal in all. There was strabismus in 2, nystagmus in 2, transient deafness in 1, facial paralysis of supranuclear type in 6. *Plantar reflexes* flexor in 6, unilateral extensor in 5, bilateral extensor in 2. *Tendon-jerks*: Lost in 2, otherwise normal or exaggerated. Never any weakness or flaccid paralysis of any muscles of trunk or extremities on admission and afterwards. All abnormal neurological signs disappeared in fourteen days or less. No sequelæ have been observed. Pyrexial course variable, from six to twelve days.

Pathological findings and investigations.—Cerebrospinal fluid: clear or faintly opalescent, often with a fine clot on standing. Cells 40 to 800, 80 to 100% mononuclears. Protein 60 to 160 mg%. Chlorides always normal. Always bacteriologically sterile. X-rays of chest and nasal sinuses and also serum and blood tests revealed nothing abnormal. Specimens of the cerebrospinal fluid from 9 patients were examined by Dr. Findlay by animal inoculation and culture for the presence of a virus and all results were negative. Specimens of serum at different stages of the illness were also examined for the development of antibodies against the virus of choriomeningitis and all results were negative.

Some of the clinical features of the two comatose cases are worthy of special mention.

The first was a boy of 4 years, admitted on the fourth day in a semiconscious condition. The next day his temperature was 105°, he could swallow a little reflexly but could not be roused, there were no convulsions, no cyanosis. The pupils were moderately dilated and reacted sluggishly to light. The tendon-jerks were all brisk, the left plantar response was extensor and remained so for three weeks. He regained consciousness four days after admission, remained irritable for a week, and was discharged after forty-five days without any sequelæ.

The fatal case was a girl of 15. While home on the third day of illness she had a generalized convulsion lasting twenty minutes. She recovered consciousness, could speak and swallow but remained dazed. On the fourth day she had another generalized convulsion lasting one hour and did not regain consciousness. She was admitted in coma with jerky movements of all four limbs, she could swallow reflexly slowly. T. 104·8°. Pupils equal, dilated, reacting sluggishly to light. Right facial paralysis, of the lower part of the face only. Abd. reflexes and tendon-jerks absent. Right plantar response extensor; left not obtained. Heart, lungs, urine, blood chemistry, nil abnormal found. Blood culture sterile. Twelve hours later coma deeper, pupils fixed, respirations shallow and rapid, colour dusky, P. 140. Continuous O_2 administered and 50% glucose I.V., the colour improved but the coma was unchanged. She died sixteen hours after admission.

In neither case was there evidence of anoxæmia previous to the onset of the coma or of the convulsions. The changes in the cerebrospinal fluid were similar to those of the other eleven cases.

Post-mortem examination of the fatal case showed intense congestion of the pia mater over the convexity of the brain and cerebellum, some generalized œdema of the brain, no purulent exudate, no hæmorrhage.

Microscopical examination showed intense infiltration of the leptomeninges over the whole of the nervous system by large mononuclear cells especially over the parietal cortex and the cerebellum, small areas of perivascular cuffing with the same type of cells in the pons, mid-brain bulb and region of the basal ganglia and similar but less marked changes in the spinal cord.

Dr. Findlay carried out exhaustive investigations with specimens of this case. Serum, cerebrospinal fluid during life and selected parts of the nervous system after death were inoculated into mice, guinea-pigs, rabbits, and rhesus monkeys. All animals remained normal.

The 13 patients came from scattered areas all over London. The youngest was 2 years old, the others between 4 and 39. No two cases came from the same household, but Dr. Conybeare in his field investigations found instances of undiagnosed febrile illness in two of the contacts of one of our patients. Not one of the 13 had been in contact with a recognized case of poliomyelitis. The clinical and pathological findings amount to this: acute sterile lymphocytic meningitis in all, symptoms of encephalitis in some, confirmed post mortem in one.

Ætiology.—I think one can safely exclude a bacterial infection and assume that a neurotropic virus was in operation. Since Wallgren's [6] publication in 1924, the existence of "aseptic" (meaning thereby non-bacterial) lymphocytic meningitis has been well recognized. Numerous examples of this condition, mostly benign, have been described, but it is evident that it never constituted one ætiological entity. The viruses of mumps, of herpes zoster, of poliomyelitis, of encephalitis lethargica, of vaccinia, of measles, &c., and, since 1934, that of Armstrong and Lillie's [1] choriomeningitis of murine origin, more recently that of glandular fever, that (or should I say those) of atypical pneumonia have all been shown to give rise at times to meningitic manifestations with lymphocytosis of the cerebrospinal fluid. One is therefore forced to the conclusion that "aseptic lymphocytic meningitis" is only the common pathological denominator of a large number of virus infections of the nervous system, and in every instance the exact ætiology has to be determined by either (1) the isolation and identification of the virus, or (2) the assessment of the clinical features and the epidemiological associations.

Dr. Findlay's totally negative findings excluded choriomeningitis in view of the facility of infecting mice with the cerebrospinal fluid, and in the one fatal case made poliomyelitis improbable. On clinical grounds: post-infectious encephalitis, encephalitis lethargica (owing to the absence of sequelæ), also glandular fever and atypical pneumonia were all most unlikely. Poliomyelitis did not suggest itself to us at the time as not one of the 13 cases had been a contact of the disease and only one case of poliomyelitis had been admitted during the same period.

In the summer of 1945 an outbreak of febrile illness associated with lymphocytic meningitis in the South-east of France was reported by Sohier and Gaubert [5] and by Brunel [2]. Recently Jennings [4] has described a number of cases of a similar illness which occurred in North-West Middlesex about the same time as ours. Not one of these authors could incriminate any specific virus with certainty.

During the present epidemic of poliomyelitis in the months of June, July and August 1947, at the same time as 24 paralytic cases, 18 patients with lymphocytic meningitis presenting no clinical evidence of lower motor neurone involvement either in brain stem or cord, were admitted. Of these 18 cases, one was unconscious four days; another, alert and conscious, had myoclonus and acute cerebellar ataxia. They all recovered without paralysis or sequelæ, and I must admit that clinically they were indistinguishable from the cases seen in the summer of 1946. Rather than postulate two viruses, it is generally assumed, and probably correctly, that these unusual cases are also due to the poliomyelitis virus with clinical manifestations at different levels of the nervous system, or alternatively, that the present virus is a new strain with a different method of attack.

Diagnosis based on epidemiological prevalence is often unsatisfactory. Between 1910 and 1913, cases of lymphocytic meningitis in Paris were credited to the virus of poliomyelitis which was then prevalent. In 1922, in Stockholm, however, they were attributed to the virus of encephalitis lethargica. Looking back on our cases of 1946, the only way that poliomyelitis could have been recognized as the offending virus would have been a systematic search for it in the fæces of the patients. The short supply of monkeys, however, precluded such a large-scale investigation. Systematic search for the virus in the stools of poliomyelitis patients, of subclinical cases with or without lymphocytic meningitis and even of their contacts has been carried out in America and has shown a very high proportion of positive results [3].

The need for some rapid and easy method of identifying viruses is becoming every day a pressing problem. In the absence of help from the virus expert, the clinician faced with an isolated case or a series of cases of primary lymphocytic meningitis or meningo-encephalitis must base his diagnosis on a fine calculation of probabilities.

REFERENCES

1 Armstrong, C., and Lillie, R. D. (1934) *Publ. Hlth. Rep. Wash.*, 49, 1019.
2 Brunel, H. (1946) *Lyon méd.*, 175, 24.
3 Casey, A. E. *et al.* (1946) *Amer. J. Dis. Child.*, 72, 661.
4 Jennings, G. H. (1947) Outbreak of Virus Encephalo-meningitis in North-West Middlesex, *Lancet*, (i), 471.
5 Sohier, R., and Gaubert, Y. (1946) *Pr. méd.*, 30, 433.
6 Wallgren, A. (1924) *Acta paediatr., Stockh.*, 4, 158.

Dr. Douglas McAlpine: *Some observations on the* 1947 *outbreak of acute poliomyelitis.*—As a result of the outbreak of poliomyelitis this year we must anticipate a higher annual incidence of the disease than heretofore, with the probability of epidemics from time to time. The total number of cases of poliomyelitis and polio-encephalitis notified this year up to the present time exceeds 6,500; the corrected figure is probably less than two-thirds of this total. It has become increasingly clear that cases occur all the year round, an important epidemiological point. A preliminary estimate from the Ministry of Health suggests that at least 20% of all notifications have been over the age of 15, a fact which confirms the upward trend in the age-incidence in other countries. The mortality figure has been a low one, probably below 10%. There is a close similarity between the constitutional symptoms of the abortive case and the prodromata that usually precede the non-paralytic and paralytic forms. This fact suggests that in the majority of individuals symptoms subside without any evidence of invasion of the nervous system. The cerebrospinal fluid is normal. The virus may be isolated from the throat and stools of such cases. This constitutes the *abortive* form. The same remark applies to carriers, but they remain symptomless. Less frequently meningeal symptoms and signs develop and the cerebrospinal fluid shows changes; this is the non-paralytic form. Lastly, in a comparatively few individuals paralysis ensues. The symptoms which should suggest an abortive attack in contacts are headache, shivering, malaise, vague body pains and fever. To all or some of these may be added catarrhal symptoms (sore throat, coryza) or gastro-intestinal symptoms (nausea, vomiting, diarrhœa).

Non-paralytic form.—As far as I can judge this form of the disease has been common, but there has been much variation in the intensity of meningeal signs. I would include under this heading those cases which, in addition to signs of meningitis, also show nystagmus but no evidence of paresis. Despite the typical picture of meningitis, the cerebrospinal fluid may be normal; such cases should during an outbreak be labelled "abortive".

The paralytic form.—It is well known that the clinical picture of poliomyelitis may vary, not only from epidemic to epidemic, but also during the course of a single epidemic. Furthermore, clinical and histological data have made it clear that although the virus shows a high degree of neurotropism for the motor cells of the cranial nerves and spinal cord, other constituents of the nervous system may not be spared. These facts go far to explain the somewhat varied clinical picture which may be met with in this disease. The present epidemic has shown no clinical features that have not been encountered in previous outbreaks in other countries, so that a description of the various types of spinal paralysis need not detain us. Rarely pyramidal signs in one or both lower limbs are associated with wasting in upper limb muscles or of intercostals and abdominal muscles, or more rarely of a muscle group in a lower limb. Sensory symptoms such as numbness or tingling may be prominent at the onset but sensory loss is transitory. Pyramidal signs and temporary sensory phenomena, though definitely uncommon, may occasionally occur in the spinal form of the disease.

Polio-encephalitis.—The signs are mainly those of a brain-stem encephalitis, but clinically and histologically higher levels of the nervous system may be affected. A somewhat unusual feature of the cases that have occurred during the past year has been a marked degree of drowsiness and mental confusion during the first few days of the illness. In my experience the commonest sign of polio-encephalitis is nystagmus. All types may be seen. It may be the only sign signifying invasion of the central nervous system; however, other signs of polio-encephalitis or spinal paralysis are usually present. During this epidemic the presence of nystagmus, photophobia and neck rigidity in a patient who has been ill for a few days with headache and fever was considered sufficient evidence for the diagnosis of polio-encephalitis although, as I have indicated earlier, in the absence of other signs, the diagnosis of "non-paralytic poliomyelitis" might be preferable. I have seen some cases with a rare form of ocular disorder which may occur alone or may be associated with emotional instability, marked tremor of the head and mild cerebellar signs.

I owe to Dr. MacKenzie, Superintendent of Groby Road Fever Hospital, Leicester, the opportunity of seeing this condition for the first time. The following is a brief résumé of the case:

M. T., female aged 13, was taken ill on September 12 with headache, low back pain and fever. During the next four days she was feverish, sleepless and delirious. September 17: Admitted to hospital. The most striking feature of the case was a gross rotatory nystagmus-like movement of the eyes accompanied by a tremor of the head. The upper limbs were tremulous, but other cerebellar signs were not conspicuous. C.S.F., 17 lymphocytes per c.mm. Protein 0·15 gm.%. On September 22 she was mentally alert, not obviously emotional and complained only of the tremor of her head. The pupils were dilated but reacted normally. There were no ocular pareses. On looking straight forward no abnormality was evident, but on the slightest movement of her eyes laterally or upwards to fix an object, the following signs appeared: (1) A coarse side-to-side tremor of both eyeballs which was maximal at first and then after a few seconds suddenly ceased even though the eyes remained fixed on the object, a feature which distinguished the condition from true nystagmus. (2) Synchronous with the eye movements and occurring simultaneously with them was a coarse side-to-side tremor of the head; this ceased at the same moment as the eye movements. Speech was normal as were the remaining cranial nerves. Except for a mild tremor of the hands on voluntary movement and slight ataxia of the left lower limb, cerebellar signs in the limbs were not conspicuous; however, gait was not examined as the patient was in bed. The deep reflexes were normal and the plantar responses were flexor.

I have seen further examples of this condition limited to the eyes. Dr. Strickland in a recent letter to the *Lancet* has described three cases showing a minor degree of the same disturbance and suggests the term "prefixation nystagmus". A case similar to the one to which I have referred was described by Marmion and Sandilands. It may signify an unusual strain of virus.

Pyramidal signs are not unusual in polio-encephalitis, an exaggerated jaw-jerk being sometimes the first sign of their presence. Associated with nystagmus and pyramidal signs, or occurring independently of them, may be found paresis of one or more of the motor cranial nerves of which the seventh is the most vulnerable. Every variety of cranial nerve palsy from an ophthalmoplegia to mild or severe bulbar paresis has been noted in the present epidemic.

Cerebrospinal fluid.—I wish to refer to two features of the cerebrospinal fluid which have not been uncommon during this outbreak: (1) A relatively normal or normal cell count; (2) a marked increase in the protein content of the fluid. In paralytic cases which I saw overseas during the war I estimated that in approximately 5% there was a normal cell count during the active stage of the disease. The combination of a low cell count and a high protein in poliomyelitis has been reported on many previous occasions.

Differential diagnosis.—The number of neurotropic viruses which attack man appear to be on the increase, but we have no knowledge of the extent to which they have invaded this country. From the continuous presence of fresh cases of post-encephalitic Parkinsonism we can assume that epidemic encephalitis is endemic in this country. However, with the virus of poliomyelitis well established a brain-stem encephalitis is much more likely to be due to this virus than that to endemic encephalitis. The majority of the cases of virus encephalomeningitis which Jennings reported from North-West Middlesex last year, had features identical with the cases of polio-encephalitis which have appeared in the London area this summer. Dr. Laurent's series of cases would also appear to fall into the same category. Unless there is good proof to the contrary, a diagnosis of polio-encephalitis should be made in any case of brain-stem encephalitis if accompanied by meningeal signs. Similarly, the commonest cause of an acute benign lymphocytic meningitis is likely to be the virus of poliomyelitis. However, it is obvious that the complexity of the subject calls for the placing of adequate facilities at the disposal of those who are working on virus research in this country.

In conclusion, I would submit that if we are to progress in our knowledge of poliomyelitis up to and beyond the point already reached by American workers, the following steps amongst others should be taken: (1) The provision of a liberal supply of animals suitable for experimental work on poliomyelitis and encephalitis. (2) The training of teams of field workers who should be at the disposal of the Ministry of Health for the purpose of investigating each fresh outbreak of the disease.

BIBLIOGRAPHY

BERTENIUS, B. S. (1947) On the Problem of Poliomyelitis, An Epidemiological Statistical Study. *Acta path. microbiol. Scand.* Supp. 68.

BURNET, F. M., and JACKSON, A. V. (1939) *Aust. J. exp. Biol. med. Sci.*, **17**, 261.

CASEY, A. E., FISHBEIN, W. I., and BUNDESEN, H. N. (1945) *J. Amer. med. Ass.*, **129**, 1141.

JENNINGS, G. H. (1947) *Lancet* (i), 471.

MARMION, D. E., and SANDILANDS, J. (1947) *Lancet* (ii), 508.

ORZECHOWSKI, K. (1927) *J. Psychol. Neurol. Lpz.*, **35**, 1.

SABIN, A. B. (1947) *J. Amer. med. Ass.*, **134**, 749.

SMITH, M. L., BRIDGE, E. M., UNDERWOOD, H. E., and DALE, G. E. (1945) *J. Amer. med. Ass.*, **129**, 1150.

STRICKLAND, B. (1947) *Lancet* (ii), 369.

Dr. F. O. MacCallum stated that suspensions of the brain and cord from 8 fatal cases of poliomyelitis and polio-encephalitis from various parts of the country had each been inoculated intracerebrally into a single rhesus monkey. Four monkeys inoculated with material from Belfast, Manchester, Carlisle and London had developed typical poliomyelitis and four had shown no sign of illness. A small number of specimens of acute and convalescent sera from recent cases of poliomyelitis had been examined for neutralizing antibody to the Lansing mouse-adapted human strain of poliomyelitis. No antibody had been detected in these sera.

Dr. H. Stanley Banks discussed the number and character of the 1946 cases of "benign lymphocytic meningitis" at the Park Hospital. In view of the 1946 experience, he could not exclude the possibility of an unknown virus being responsible for at least some of this year's non-paralytic cases with meningeal reactions, and suggested that "*primary* lymphocytic meningitis" should be made notifiable by hospital medical staff.

Dr. W. H. Kelleher: The Western Hospital received a high proportion of bulbar types of poliomyelitis (30%) in the earlier weeks of the epidemic and in a few of these there was some drowsiness. In one case, with marked cranial nerve disturbances and mid-brain and cerebellar involvement, there developed deep unconsciousness for a comparatively brief period—less than twenty-four hours. There was no doubt left in the minds of those who observed our cases that they were poliomyelitis and that in no case could a suspicion of meningo-encephalitis of other virus ætiology be sustained.

In only one-half of the 170 cases admitted to the Western Hospital this year could the diagnosis of poliomyelitis be confirmed. Of the first 66 genuine cases only 33% were under 5 years, 40% were between 5 and 15 years and 27% were over 15 years. Those with paresis or paralysis of a limb or limbs amounted to 63%, which compares favourably with the 91% of this type of case admitted in 1938—the previous highest incidence year. More significantly, only 19% had an upper and lower limb or limbs affected as compared with 56% in 1938. 30% of our cases showed disturbance of cranial nerves. Facial paralysis was noted in 8% (1% in 1938). Considering the number with bulbar lesions we were fortunate in meeting with not more than two patients with involvement of the vital centres, both of whom died. The number of cases with paralysis of diaphragm and/or intercostals was appreciably less than in 1938, which was in conformity with the lessened incidence of spinal lesions in general.

Dr. M. Mitman: Mr. Nissen mentioned the outbreak of influenza which preceded his epidemic of poliomyelitis. The close association of one virus disease with another or of one virus disease with a bacterial one might have profound epidemiological significance. Surveying well-known associations, Dr. Mitman mentioned the pneumococcal, streptococcal and other bacterial infections complicating such virus diseases as the common cold, measles, influenza and smallpox, and contributing materially to their fatality; the activation of febrile herpes by pneumonia, meningococcal meningitis and other diseases; but his chief interest lay in the epidemiological importance of the common cold as a precursor of epidemics of bacterial and virus diseases. A "cold" was a recognized antecedent of a number of diseases and, in trying to assess its importance, it was essential to distinguish 3 similar syndromes: First, a common cold of virus ætiology; secondly, the prodromal coryzal symptoms of the disease proper; and, thirdly, the illness of infection. Is there an illness of infection due to the specific organism of the disease or does this preliminary febrile disorder represent a different infection? Could it, for example, be a "common cold" capable of influencing the invasion of the individual and the herd with the specific organism? In the individual there is evidence that a "cold" can prepare the soil for invasion by the specific organism. In the herd it could allow the more ready dissemination of the specific organism through a large number of hosts, and in this way allow an epidemic variant to appear and to spread. It is likely that such a variant is a necessary preliminary to many epidemics. In poliomyelitis interest in this connexion devolves upon the dromedary type of temperature and the significance of the upper respiratory symptoms associated with the first pyrexial hump. Are they due to an illness of infection (and therefore possibly due to a different infection), or are they prodromal symptoms of the disease proper? He accepted the latter view, but felt that outbreaks of respiratory infection, like the influenza reported by Mr. Nissen, preceding epidemics of nervous disease, were worth close study.

Dr. Jan Jaworski said that in Poland he had treated 2 cases of poliomyelitis by injecting 3-6 c.c. of the patient's own blood subcutaneously over the region of C. 3 and 4 and again over L. 3 and 4.

Both patients were cured by six injections.

This treatment was similar to that which he had employed with success in the treatment of herpes zoster.

A paper on Acute Anterior Poliomyelitis by Sir ALLEN DALEY (Section of Medicine, November 25, 1947) will appear in the January *Proceedings*.

INDEX

PROCEEDINGS OF THE ROYAL SOCIETY OF MEDICINE, VOL. XL, 1946-1947

INDEX

VOL. XL, 1946-7

Note.—In this volume two series of numbers are used for pagination, one being the sectional page number and the other the volume page number. The latter only is used in the Index

abdominal incisions, packing of, in peritonitis (I. Lewis), 652
  wall, nodules in, ? fibrosarcoma (A. C. Roxburgh), 259
abdomino-perineal operations for cancer of rectum, anæsthesia for (*Discussion*), 263
Abel, A. L., carcinoma of the paroophoron, invading the rectum, 834
able-bodiedness (H. E. Griffiths), 293
accident service, physiotherapy in (Sir M. Page), 15
aclasis, diaphyseal (G. O. Tippett), 485
acne conglobata (L. Forman), 699
Adams, A. W., epididymoma; histology: old hæmatoma (*By title*), 810
  hypoplastic kidney and hyperpiesia (*By title*), 433
  preputial fistula (*By title*), 433
adenoma, chromophobe, in man of 67 (S. L. Simpson), 151
    in youth of 15 (S. L. Simpson), 151
  of rectum, difference from papilloma explained (C. E. Dukes), 829
  sebaceum (H. W. Gordon), 700
adrenal cortex, overactivity of (*Discussion*), 35
airborne infections, modern methods of control (*Discussion*), 381
Alajouanine, Th., cerebral œdema (*Disc.*), 686
Alexander, J. M. (for W. G. Wyllie), exophthalmic goitre, 546
    neurofibromatosis, 546
    pseudo-hypertrophic muscular dystrophy, 546
Allen, H. W., ? epidermodysplasia of Lewandowski and Lutz: ? abortive form of blastomycosis or chromoblastomycosis, 251
allergy in ophthalmology (*Discussion*), 578
Alston, J. M., modern methods in the control of airborne infections (*Disc.*), 383
anæmia, hypoplastic (I. A. B. Cathie), 545
anæsthesia and shock (*Discussion*), 167
  for Cæsarean section (*Discussion*), 557
  in children (*Discussion*), 540
  inhalation, development in later nineteenth century (B. Duncum), 68
  skin temperature as clinical aid during (J. Clutton-Brock), 607
analgesia, local (*Discussion*), 525
analgesic drugs, chemistry and pharmacology of (F. Prescott), 527
Andrewes, C. H., Bradley, W. H., Chalmers, D. K. M., and Fulton, F., common cold: interim report on a transmission experiment, 632
aneurysm, carotid-cavernous, spontaneous (S. P. Meadows), 554
  cirsoid (K. W. Priddis), 121
  intracranial, oculomotor palsy caused by (G. Jefferson), 419
anorectal region, congenital anomalies (*Discussion*), 876
antro-atticotomy in tympanomastoid suppuration (A. Tumarkin), 761
arachnodactyly with colobomata of lenses and choroid (R. C. Davenport), 821
Archer, G. E., the treatment of subacute maxillary sinusitis, especially in children, 854, 858
Armytage, V. B. G-, see Green-Armytage, V. B.
arteritis, temporal (M. Kremer), 84
arthrodesis of hip, Brittain method (H. H. Langston), 895
Aserman, D., anæsthesia in children (*Disc.*), 542
asthma, eczema and cataract associated (A. S. Philps), 817
Atkins, H. J. B., the management of patients with essential hypertension (*Disc.*), 778
  post-operative thrombosis (*Disc.* on Thrombosis), 193
attico-antrotomy in tympanomastoid suppuration (A. Tumarkin), 761
Aylett, S. O., advanced carcinoma of the bladder excised by perineo-abdominal cystectomy (hydronephrosis and pyonephrosis) (*By title*), see Hunt, A.

Badenoch, A. W., hairpin in male bladder (*By title*), 433
  X-ray of paper clip in wall of male bladder (*By title*), 433
  X-ray of pencil in female bladder (*By title*), 433
Bailey, E. T., typhoid osteitis of the long bones, 486

Brock, R. C., the treatment of acute empyema (*Disc.* on Treatment of non-tuberculous empyema), 645
Brody, M. B., leucotomy as an instrument of research (*Disc.*), 149
bronchial lesions, value of tomography (S. Nowell), 399
  neoplasms (P. H. Holinger) (*Film*), 858
  sarcoma (I. Lewis), 119
bronchitis, chronic, polycythæmia and papillœdema (S. P. Meadows), 555
Brooksby, J. B., the serum proteins of the domestic animals, 187
Broster, L. R., adreno-genital syndrome: the results of unilateral adrenalectomy (*Disc.* on Overactivity of the adrenal cortex), 35
Brown, L. G. (*Disc.*), 283, 285
  anterior ethmoidal hæmorrhage (*Disc.*), 283
Brown, W. G. S.-, see Scott-Brown, W. G.
Bull, J. W. D., disseminated ossified nodules in the lungs associated with mitral stenosis (*Disc.*), 408
  Paget's disease of the skull with platybasia, 85
Burn, J. L., modern methods in the control of airborne infections (*Disc.*), 383
Burrows, N. F. E. (for B. E. Schlesinger), cystic disease of bone, 538
  (for W. G. Wyllie), precocious puberty of ? suprarenal origin, 154
    primary hyperplasia of the parathyroids in a boy aged 8 years, 154
    Sturge-Weber syndrome, 546
Burt, Sir Cyril, the morphological level of personality (*Disc.*), 307
Butler, W., whooping cough and measles: an epidemiological concurrence and contrast, 384

Cade, Sir Stanford, the treatment of cancer of the tongue (*Disc.*), 409
cæcum, carcinoma associated with carcinoid tumour of small intestine (C. N. Morgan), 874
Cæsarean section, anæsthesia for (*Discussion*), 557
Cairns, Sir Hugh, penicillin in suppurative conditions of the brain and meninges (*Disc.* on Penicillin in neurology), 681
calciferol, effect on lupus vulgaris, lupus pernio and Boeck's sarcoid (I. R. Marre), 10
calcinosis universalis (A. P. Norman), 160
calculi, renal, problems (R. H. O. B. Robinson), 201
Callow, R. K., overactivity of the adrenal cortex (*Disc.*), 46
Calvé-Legg-Perthes' disease (H. G. Korvin), 886
Cameron, G. R., blood of normal goats (*Chart*), 192
  sudden shifts of body fluids (*Pres. address*), 1
Campbell, D., illumination (*Disc.*), 828
cancer of larynx, review (V. E. Negus), 515
  of tongue, treatment of (*Discussion*), 409
Capps, F. C. W., otology in school children and child welfare (*Disc.*), 107
  recurrent chondroma of the subglottic region, 285
carcinoma of cæcum associated with carcinoid tumour of small intestine (C. N. Morgan), 874
  of cervix, surgical and radiological treatment (*Discussion*), 907
  of colon and rectum associated (F. Forty), 872
  of hepatic flexure of colon (R. W. Raven), 876
  of rectum with secondary in liver (O. V. Lloyd-Davies), 875
  of thyroid (J. M. Graham and R. McWhirter), 669
Carmichael, E. A., myoclonus, 553
Carver, J. H., achalasia of the uretero-vesical orifice and pyelitis of pregnancy (*By title*), 433
  calcification of kidney and ureter (X-rays) (*By title*), 810
cataract, asthma and eczema associated (A. S. Philps), 817
  diabetic (A. Lister), 130
  endocrine (A. Lister), 130
Cathie, I. A. B., hypoplastic anæmia, 545
Cave, J. N., anæsthesia for Cæsarean section (*Disc.*), 566
Cawadias, A. P., clinical science in the light of history, 453
Cawthorne, T., review of surgery of otosclerosis, 320, 328
  transmeatal attico-antrotomy in chronic tympanomastoid suppuration (*Disc.*), 771
cerebral fossa, middle, tumours of (E. Lindgren), 859
  œdema (*Discussion*), 686
cervical vertebræ, injuries (V. H. Ellis), 19
cervix, carcinoma, surgical and radiological treatment (*Discussion*), 907
Chalmers, D. K. M. (with C. H. Andrewes, W. H. Bradley, and F. Fulton), common cold: interim report on a transmission experiment, 632
Chesser, E., birth control: some medical and legal aspects (*Disc.*), 346
chest injury, rehabilitation in (*Discussion*), 287
children, ear affections in (H. V. Forster), 101
choanal atresia (T. M. Boyle), 283
Cholmeley, J. A., chondro-osteodystrophy: ? Morquio, 491
  chronic osteomyelitis: multiple foci including spine (*By title*), 885
  gross shortening of leg and deformity of knee associated with tuberculous disease of the hip (*By title*), 885
chondroma, recurrent, of subglottic region (F. C. W. Capps), 285
chondro-osteodystrophy (J. A. Cholmeley), 491
choroidal neoplasm (G. G. Penman), 819
choroiditis, tuberculous (A. S. Philps), 817
cirrhosis, juvenile (U. James), 162
Clarke, W. E. (for E. C. Warner), dermatomycosis, 475
clinical science in the light of history (A. P. Cawadias), 453
Cloake, P. C. P. (*Disc.*), 85, 87
Clutton-Brock, J., skin temperature as a clinical aid during anæsthesia, 607
Coats's disease (M. L. Hine), 818

Baker, A. H., X-ray treatment of osteomyelitis of the fingers (*Disc.* on X-ray treatment of inflammatory diseases), 111

Banks, H. S., anterior poliomyelitis (*Disc.*), 931
  the present status of infectious disease control in continental Europe (*Disc.*), 627

Barber, H. W. (*Disc.*), 477
  multiple tuberculides, including the scleroma-like form of erythema induratum, 245
  ulcer of vulva in young girl (*Disc.*), 245

basal ganglia, angioma of (L. J. Rowley), 164

basophilism treated successfully with radon seeds (A. C. Crooke), 153

Batchelor, J. S., excision head and neck of femur and sub-trochanteric osteotomy for irreducible fracture dislocation of the hip: two males aged 20 and 22 respectively (*By title*), 885
  excision head and neck of femur and sub-trochanteric osteotomy for pyogenic arthritis of the hip: child aged 9 (*By title*), 885
  excision head and neck of femur and sub-trochanteric osteotomy for unilateral osteo-arthritis of the hip: female aged 40 (*By title*), 885
  X-ray films of two cases showing an unusual form of osteochondritis of the patella in adolescent males (*By title*), 885

Bateman, G. H., bronchial neoplasms (*Film*), see Holinger, P. H.

Bauwens, P., the complex behaviour of high-frequency currents in simple circuits, 741

Beck, D. K., dystonia musculorum deformans with another case in the same family, 551

Bedford, D. E., the management of patients with essential hypertension (*Disc.*), 779

Bedson, S. P., the laboratory diagnosis of virus infections (*Disc.*), 662

Behrman, S., arteritis of the temporal vessels associated with loss of vision, 569

Bell, A. D. C., dermatomyositis in a child, 481

Bell, J. G. Y., the use of penicillin in urology (*Disc.*), 441

Bennet, E. A., the social aspects of homosexuality (*Disc.*), 585

Berlin at the time of occupation (P. G. Horsburgh), 93

Bettley, F. R. (*Disc.*), 505
  miliary lymphocytoma, 13
  polymorphic light eruption, 261

bile, penicillin concentration in (E. G. Tuckwell), 654

Birt, St. J. M. C. (with T. W. Mimpriss), bladder neck dysfunction (*By title*), 809
  transurethral resection in a patient of 80 (*By title*), 809
  tumour for diagnosis (*By title*), 809
  two cases of imperfect descent of the testicle (*By title*), 809
  unusual ulcer of the bladder (*By title*), 809

birth control: some medical and legal aspects (*Discussion*), 51, 346

bladder, distension, physiological disturbances from (D. Whitteridge), 229
  injuries (R. A. Mogg), 795
  paralysis due to spinal cord injuries (*Discussion*), 219

? blastomycosis, abortive form (H. W. Allen), 251

Blomfield, G. W., some aspects of surgical and radiological treatment of carcinoma of the cervix (*Disc.*), 917

blood disorders, inherited, in rodents (H. Grüneberg), 191
  normal human, constituents of (C. L. Oakley), 190

blue nævus in mongolian patch (C. L. Collins), 505

Bodenham, D. C., technique and value of tattooing in plastic surgery (*Disc.*), 883

body fluids, sudden shifts (G. R. Cameron), 1

Boeck's sarcoid, treatment with calciferol (I. R. Marre), 11

bone, cystic disease (N. F. E. Burrows), 538
  deformity associated with multiple neurofibromatosis (N. C. Tanner), 47
  tumours, experience with (J. F. Brailsford), 787

Bourne, A. W., birth control: some medical and legal aspects (*Disc.*), 52

Bourne, W. A., sclerodactylia with œsophageal lesion (3 cases), 463

Boyd, R., birth control: some medical and legal aspects (*Disc.*), 57

Boyle, T. M., choanal atresia, 283

Bradley, W. H. (with C. H. Andrewes, D. K. M. Chalmers, and F. Fulton), common cold: interim report on a transmission experiment, 632

Brailsford, J. F., some experiences with bone tumours, 787

Brain, R. T. (with M. M. White), ulcer of vulva in young girl, 243

Brain, W. R. and Wright, A. D., compression neuritis of both median nerves in the carpal tunnel: surgical decompression: Klippel-Feil deformity of neck: Sprengel shoulder, 83

brain, œdema (*Discussion*), 686
  researches due to leucotomy (*Discussion*), 141

breast, lactating, histology of (S. Engel), 899
  physiology, recent developments in knowledge of (*Discussion*), 899

breathing machines as used in Sweden and Denmark (E. T. Moerch), 603

Bride, T. M., congenital coloboma of the iris and choroid, with cataracts, left intracapsular extraction (*By title*), see Scott, R. S.
  infantile glaucoma in a child of 3 months—bilateral iridectomy (*By title*), see Scott, R. S.
  retinitis pigmentosa with bitemporal hemianopia (*By title*), see Scott, R. S.
  right and left iridocyclitis, ? sympathetic (*By title*), see Scott, R. S.

Brinton, D. H., Wilson's disease, 556

Brittain method of arthrodesis of hip (H. H. Langston), 895

Britton, C. J. C., allergy in ophthalmology (*Disc.*), 578, 582

Brock, J. C., see Clutton-Brock, J.

Brock, R. C., the treatment of acute empyema (*Disc.* on Treatment of non-tuberculous empyema), 645
Brody, M. B., leucotomy as an instrument of research (*Disc.*), 149
bronchial lesions, value of tomography (S. Nowell), 399
  neoplasms (P. H. Holinger) (*Film*), 858
  sarcoma (I. Lewis), 119
bronchitis, chronic, polycythæmia and papillœdema (S. P. Meadows), 555
Brooksby, J. B., the serum proteins of the domestic animals, 187
Broster, L. R., adreno-genital syndrome: the results of unilateral adrenalectomy (*Disc.* on Overactivity of the adrenal cortex), 35
Brown, L. G. (*Disc.*), 283, 285
  anterior ethmoidal hæmorrhage (*Disc.*), 283
Brown, W. G. S.-, see Scott-Brown, W. G.
Bull, J. W. D., disseminated ossified nodules in the lungs associated with mitral stenosis (*Disc.*), 408
  Paget's disease of the skull with platybasia, 85
Burn, J. L., modern methods in the control of airborne infections (*Disc.*), 383
Burrows, N. F. E. (for B. E. Schlesinger), cystic disease of bone, 538
  (for W. G. Wyllie), precocious puberty of ? suprarenal origin, 154
  primary hyperplasia of the parathyroids in a boy aged 8 years, 154
  Sturge-Weber syndrome, 546
Burt, Sir Cyril, the morphological level of personality (*Disc.*), 307
Butler, W., whooping cough and measles: an epidemiological concurrence and contrast, 384

Cade, Sir Stanford, the treatment of cancer of the tongue (*Disc.*), 409
cæcum, carcinoma associated with carcinoid tumour of small intestine (C. N. Morgan), 874
Cæsarean section, anæsthesia for (*Discussion*), 557
Cairns, Sir Hugh, penicillin in suppurative conditions of the brain and meninges (*Disc.* on Penicillin in neurology), 681
calciferol, effect on lupus vulgaris, lupus pernio and Boeck's sarcoid (I. R. Marre), 10
calcinosis universalis (A. P. Norman), 160
calculi, renal, problems (R. H. O. B. Robinson), 201
Callow, R. K., overactivity of the adrenal cortex (*Disc.*), 46
Calvé-Legg-Perthes' disease (H. G. Korvin), 886
Cameron, G. R., blood of normal goats (*Chart*), 192
  sudden shifts of body fluids (*Pres. address*), 1
Campbell, D., illumination (*Disc.*), 828
cancer of larynx, review (V. E. Negus), 515
  of tongue, treatment of (*Discussion*), 409
Capps, F. C. W., otology in school children and child welfare (*Disc.*), 107
  recurrent chondroma of the subglottic region, 285
carcinoma of cæcum associated with carcinoid tumour of small intestine (C. N. Morgan), 874
  of cervix, surgical and radiological treatment (*Discussion*), 907
  of colon and rectum associated (F. Forty), 872
  of hepatic flexure of colon (R. W. Raven), 876
  of rectum with secondary in liver (O. V. Lloyd-Davies), 875
  of thyroid (J. M. Graham and R. McWhirter), 669
Carmichael, E. A., myoclonus, 553
Carver, J. H., achalasia of the uretero-vesical orifice and pyelitis of pregnancy (*By title*), 433
  calcification of kidney and ureter (X-rays) (*By title*), 810
cataract, asthma and eczema associated (A. S. Philps), 817
  diabetic (A. Lister), 130
  endocrine (A. Lister), 130
Cathie, I. A. B., hypoplastic anæmia, 545
Cave, J. N., anæsthesia for Cæsarean section (*Disc.*), 566
Cawadias, A. P., clinical science in the light of history, 453
Cawthorne, T., review of surgery of otosclerosis, 320, 328
  transmeatal attico-antrotomy in chronic tympanomastoid suppuration (*Disc.*), 771
cerebral fossa, middle, tumours of (E. Lindgren), 859
  œdema (*Discussion*), 686
cervical vertebræ, injuries (V. H. Ellis), 19
cervix, carcinoma, surgical and radiological treatment (*Discussion*), 907
Chalmers, D. K. M. (with C. H. Andrewes, W. H. Bradley, and F. Fulton), common cold: interim report on a transmission experiment, 632
Chesser, E., birth control: some medical and legal aspects (*Disc.*), 346
chest injury, rehabilitation in (*Discussion*), 287
children, ear affections in (H. V. Forster), 101
choanal atresia (T. M. Boyle), 283
Cholmeley, J. A., chondro-osteodystrophy: ? Morquio, 491
  chronic osteomyelitis: multiple foci including spine (*By title*), 885
  gross shortening of leg and deformity of knee associated with tuberculous disease of the hip (*By title*), 885
chondroma, recurrent, of subglottic region (F. C. W. Capps), 285
chondro-osteodystrophy (J. A. Cholmeley), 491
choroidal neoplasm (G. G. Penman), 819
choroiditis, tuberculous (A. S. Philps), 817
cirrhosis, juvenile (U. James), 162
Clarke, W. E. (for E. C. Warner), dermatomycosis, 475
clinical science in the light of history (A. P. Cawadias), 453
Cloake, P. C. P. (*Disc.*), 85, 87
Clutton-Brock, J., skin temperature as a clinical aid during anæsthesia, 607
Coats's disease (M. L. Hine), 818

Cochrane, J. B., anæsthesia for Cæsarean section (*Disc.*), 568
Cohen, E. L. (*Disc.*), 704
  allergy in ophthalmology (*Disc.*), 581
  treatment of the lymphadenopathies (*Disc.*), 621
Cohen, H., rheumatic diseases: a challenge and an opportunity (Samuel Hyde Memorial Lecture), 443
cold, common, interim report on transmission experiment (C. H. Andrewes, W. H. Bradley, D. K. M. Chalmers and F. Fulton), 632
colectomy (E. G. Muir), 831
colitis, chronic ulcerative, specimen of colon removed (R. S. Corbett), 871
Collard, P., and Nevin, S., affection of the trigeminal nerve nucleus and central grey matter of the spinal cord following the administration of stilbamidine, 87
Colledge, L. (*Disc.*), 284
  ophthalmo-neurological symptoms in malignant nasopharyngeal tumours (*Disc.*), 138
Collier, J., emergency epistaxis, 277
Collins, C. L., blue nævus in a mongolian patch, 505
coloboma of lenses and choroid, and arachnodactyly (R. C. Davenport), 821
  of optic disc, bilateral (H. L. Hughes), 821
colon and rectum, carcinoma of (F. Forty), 872
Coltart, W. D., congenital deformity of lumbar vertebræ with sciatic nerve lesion (*By title*), 492
  multiple disseminated calcinosis (*By title*), 492
Colyer, Sir Frank, notes on ten Romano-British skulls from a burial ground at Compton, Berkshire, 837
comedones, grouped, in hitherto undescribed hereditary ectodermal dysplasia (C. H. Whittle), 251
Compton burial ground, Romano-British skulls from (Sir F. Colyer), 837
convulsions due to intracranial hæmangioma (M. W. West), 164
Cook, F., some aspects of surgical and radiological treatment of carcinoma of the cervix (*Disc.*), 922
Coope, P. J. (for J. C. R. Hindenach), tuberculous abscess formation following penicillin therapy, 161
Cope, R. W., anæsthesia in children (*Disc.*), 540
Copeman, W. S. C., the ætiology of chronic rheumatism (*Disc.*) 329
Corbett, R. S., specimen of colon removed on account of severe pyoderma from a long-standing case of chronic ulcerative colitis, 871
coronary disease, shoulder pain and disability in (A. Schott), 733
Corsi, H. (*Disc.*), 26, 482
  erythematous initial tuberculide (*Disc.*), 257
  lichen planus in a boy aged 8 years, 477
  (with G. B. Mitchell-Heggs and K. D. Crow), erythrodermia in lymphatic leukæmia (malignant erythrodermia), 249
Cotchin, E., some glandular tumours of the dog, 636
Court, D., a consideration of acute intussusception in relation to medical teaching (*By title*), 550
Creer, W. S., some points about the Monteggia fracture, 241
Cripps, M. E., the effect of X-radiation on the eye from its clinical aspects (*Disc.* on X-ray treatment of inflammatory diseases), 109
Critchley, M., paraplegic eunuch with lues, 552
  post-encephalic Parkinsonism with marked palilalia, 552
Crooke, A. C., the altered physiological activity in hyperfunction of the adrenal cortex (*Disc.* on Overactivity of the adrenal cortex), 43
  basophilism treated unsuccessfully with massive doses of œstrogens and deep X-ray therapy, but cured by radon seeds inserted into the sella turcica, 153
  case for diagnosis: ? diabetes mellitus with diabetes insipidus, 153
  the treatment of toxic goitre (*Disc.*), 616
Crooks, J., the treatment of subacute maxillary sinusitis, especially in children (*Disc.*), 857
Crosland, J. H., physiotherapy in an accident service (*Disc.*), 18
Crow, K. D. (with G. B. Mitchell-Heggs and H. Corsi), erythrodermia in lymphatic leukæmia (malignant erythrodermia), 249
Crowe, H. W., osteo-arthritis of the hip-joint treated by intra-articular injections, 486
Cruickshank, R., modern methods in the control of airborne infections (*Disc.*), 381
Cruise, Sir Richard, ophthalmo-neurological symptoms in malignant nasopharyngeal tumours (*Disc.*), 138
Cullen, T. H. (for E. W. Riches), congenital hydronephrosis of unusual type (*By title*), 809
Cunliffe, A. C., modern methods in the control of airborne infections (*Disc.*), 383
curare, further experiences with (*Discussion*), 593
Currie, J. G. D., illumination (*Disc.*), 822
Curtis, F. R., venereal disease control in Denmark, Sweden and the British-occupied zone of Germany (*Disc.* on The present status of infectious disease control in continental Europe), 630

dacryocystorhinostomy (B. Reeves), 285
Dale, H. W. L., anæsthesia for abdomino-peritoneal operations for cancer of the rectum (*Disc.*), 269
  shock, with special reference to anæsthesia (*Disc.*), 178
Darier's disease and generalized pruritus (L. Forman), 8
Davenport, R. C. (*Disc.*), 818
  a family showing arachnodactyly with colobomata of lenses and choroid, 821
Davidson, M., birth control: some medical and legal aspects (*Disc.*), 51
Davies, O. V. Ll.-, see Lloyd-Davies, O. V.
Davies, W. W. W.-, see Wiggins-Davies, W. W.
Davis, D. R., disorders of skill: an experimental approach to some problems of neurosis, 583

Davis, E. D. D. (*Disc.*), 284
anterior ethmoidal hæmorrhage (*Disc.*), 282
the diagnosis and treatment of tumours of the nasopharynx, 135, 137, 707
otology in school children and child welfare (*Disc.*), 107
Dawkins, C. J. M., anæsthesia for Cæsarean section (*Disc.*), 564
further experiences with curare (*Disc.*), 601
Dawson, G. D. (*Disc.*), 553
D.D.T., malaria control with (J. M. Vine), 841
deafness, inner ear, and hypothyroidism (L. Rau), 468
Debono, J. E., kala-azar in infancy, 155, 159
Denham, P., the management of the normal third stage of labour and of hæmorrhage therein (*Disc.*), 373
Denig's operation, see trachoma
dental handpieces, sterilization (W. Harvey, C. H. LeMay and C. W. Shuttleworth), 507
dermatitis bullosa striata pratensis (H. G. Lee), 14
dermatological complications of open wounds (I. B. Sneddon), 883
dermatomyositis (W. E. Clarke), 475
in a child (A. D. C. Bell), 481
dermoid cyst simulating neoplasm of lacrimal gland (G. G. Penman), 820
Desmond, A. M., gunshot wound of the ureter (introduced by H. K. Vernon) (*By title*), 810
de Wesselow, O. L. V., xanthomatosis, see Petch, C. P.
diabetes insipidus (B. W. Powell), 544
mellitus with diabetes insipidus (A. C. Crooke), 153
Diamond, L. K., erythroblastosis fœtalis or hæmolytic disease of the newborn, 546
diaphyseal aclasis (G. O. Tippett), 485
Dicker, S. E. (with H. Heller), some renal effects of experimental dietary deficiencies, 351
dietary deficiencies, renal effects (H. Heller and S. E. Dicker), 351
Dimsdale, H., tuberose sclerosis with intracranial calcification and lesions of bone, 81
Dobbs, R., hyperelasticity of skin, see Kingsley-Pillers, E. M.
Dodd, H., cysts in the lower lobe of the kidney (*By title*), 810
diverticulum of the bladder (two cases: one male, one female) (*By title*), 433
local analgesia (*Disc.*), 531
unusual tumour of the bladder (a granuloma) (*By title*), 810
dog, glandular tumours (E. Cotchin), 636
Donald, I., uterine rupture, 379
Donovan, H., an "early" renal cancer showing calcification (*By title*), 433
uretero-colic anastomosis (*By title*), 433
the use of penicillin in urology (*Disc.*), 442
Douglas, W. R., the treatment of cancer of the tongue (*Disc.*), 415
Dowling, G. B. (*Disc.*), 506
Downie, A. W., laboratory diagnosis of smallpox (*Disc.* on The laboratory diagnosis of virus infections), 657
Doyne, P. G., familial dystrophy of cornea (*By title*), 569
Drought, C. W.-, see Worster-Drought, C.
Dudgeon, J. A., the laboratory diagnosis of influenza (*Disc.* on The laboratory diagnosis of virus infections), 660
Duke-Elder, Sir Stewart (*Disc.*), 131, 821
ophthalmo-neurological symptoms in malignant nasopharyngeal tumours (*Disc.*), 137
Dukes, C. E., an explanation of the difference between a papilloma and an adenoma of the rectum, 829
Duncum, B., the development of inhalation anæsthesia in the second half of the nineteenth century, 68
Duthie, O. M., fulminating exophthalmic ophthalmoplegia (*By title*), 432
iris inclusion—intracapsular extraction of lens (*By title*), 432
pigmentation of conjunctiva (*By title*), 432
undifferentiated malignant neoplasm of inner canthal region (*By title*), 432
dwarfism, pituitary, with toxic goitre (A. W. Spence), 151
dystonia musculorum deformans, familial (D. K. Beck), 551

Eames, J. W., the treatment of syphilis with penicillin (*Disc.*), 815
ear, affections of, in school children (H. V. Forster), 101
East, Sir W. Norwood, the social aspects of homosexuality (*Disc.*), 590
ectodermal dysplasia, hereditary, hitherto undescribed (C. H. Whittle), 251
eczema, asthma and cataract associated (A. S. Philps), 817
Edwards, C. C. (*Disc.*), 87
elbow-joint, recurrent dislocation (D. Wainwright), 885
Elder, Sir S. D.-, see Duke-Elder, Sir Stewart
electroencephalographic studies following leucotomy (G. D. Greville and S. L. Last), 145
Elkeles, A., disseminated ossified nodules in the lungs associated with mitral stenosis, 405 (*bis*)
osteoporosis circumscripta and leontiasis ossea faciei associated with Paget's disease, 466
Ellinger, P., nutritional liver disease in West Indian infants (*Disc.*), 351
Elliott, F. A., pain in the upper limb, excluding shoulder lesions (*Disc.*), 496
Ellis, V. H., injuries of the cervical vertebræ (*Pres. address*), 19
Ellman, P., the ætiology of chronic rheumatism (*Disc.*), 332
emphysema, polycythæmia and papillœdema (S. P. Meadows), 555
empyema, non-tuberculous, treatment of (*Discussion*), 645
Engel, S., histology of the lactating breast (*Disc.* on Some recent developments in knowledge of the physiology of the breast), 899
? epidermodysplasia verruciformis (H. W. Allen), 251
epidermolysis bullosa dystrophica (C. W. F. McKean), 705
epiphora following dacryocystitis (B. Reeves), 285

Cochrane, J. B., anæsthesia for Cæsarean section (*Disc.*), 568
Cohen, E. L. (*Disc.*), 704
  allergy in ophthalmology (*Disc.*), 581
  treatment of the lymphadenopathies (*Disc.*), 621
Cohen, H., rheumatic diseases: a challenge and an opportunity (Samuel Hyde Memorial Lecture), 443
cold, common, interim report on transmission experiment (C. H. Andrewes, W. H. Bradley, D. K. M. Chalmers and F. Fulton), 632
colectomy (E. G. Muir), 831
colitis, chronic ulcerative, specimen of colon removed (R. S. Corbett), 871
Collard, P., and Nevin, S., affection of the trigeminal nerve nucleus and central grey matter of the spinal cord following the administration of stilbamidine, 87
Colledge, L. (*Disc.*), 284
  ophthalmo-neurological symptoms in malignant nasopharyngeal tumours (*Disc.*), 138
Collier, J., emergency epistaxis, 277
Collins, C. L., blue nævus in a mongolian patch, 505
coloboma of lenses and choroid, and arachnodactyly (R. C. Davenport), 821
  of optic disc, bilateral (H. L. Hughes), 821
colon and rectum, carcinoma of (F. Forty), 872
Coltart, W. D., congenital deformity of lumbar vertebræ with sciatic nerve lesion (*By title*), 492
  multiple disseminated calcinosis (*By title*), 492
Colyer, Sir Frank, notes on ten Romano-British skulls from a burial ground at Compton, Berkshire, 837
comedones, grouped, in hitherto undescribed hereditary ectodermal dysplasia (C. H. Whittle), 251
Compton burial ground, Romano-British skulls from (Sir F. Colyer), 837
convulsions due to intracranial hæmangioma (M. W. West), 164
Cook, F., some aspects of surgical and radiological treatment of carcinoma of the cervix (*Disc.*), 922
Coope, P. J. (for J. C. R. Hindenach), tuberculous abscess formation following penicillin therapy, 161
Cope, R. W., anæsthesia in children (*Disc.*), 540
Copeman, W. S. C., the ætiology of chronic rheumatism (*Disc.*) 329
Corbett, R. S., specimen of colon removed on account of severe pyoderma from a long-standing case of chronic ulcerative colitis, 871
coronary disease, shoulder pain and disability in (A. Schott), 733
Corsi, H. (*Disc.*), 26, 482
  erythematous initial tuberculide (*Disc.*), 257
  lichen planus in a boy aged 8 years, 477
  (with G. B. Mitchell-Heggs and K. D. Crow), erythrodermia in lymphatic leukæmia (malignant erythrodermia), 249
Cotchin, E., some glandular tumours of the dog, 636
Court, D., a consideration of acute intussusception in relation to medical teaching (*By title*), 550
Creer, W. S., some points about the Monteggia fracture, 241
Cripps, M. E., the effect of X-radiation on the eye from its clinical aspects (*Disc.* on X-ray treatment of inflammatory diseases), 109
Critchley, M., paraplegic eunuch with lues, 552
  post-encephalic Parkinsonism with marked palilalia, 552
Crooke, A. C., the altered physiological activity in hyperfunction of the adrenal cortex (*Disc.* on Overactivity of the adrenal cortex), 43
  basophilism treated unsuccessfully with massive doses of œstrogens and deep X-ray therapy, but cured by radon seeds inserted into the sella turcica, 153
  case for diagnosis: ? diabetes mellitus with diabetes insipidus, 153
  the treatment of toxic goitre (*Disc.*), 616
Crooks, J., the treatment of subacute maxillary sinusitis, especially in children (*Disc.*), 857
Crosland, J. H., physiotherapy in an accident service (*Disc.*), 18
Crow, K. D. (with G. B. Mitchell-Heggs and H. Corsi), erythrodermia in lymphatic leukæmia (malignant erythrodermia), 249
Crowe, H. W., osteo-arthritis of the hip-joint treated by intra-articular injections, 486
Cruickshank, R., modern methods in the control of airborne infections (*Disc.*), 381
Cruise, Sir Richard, ophthalmo-neurological symptoms in malignant nasopharyngeal tumours (*Disc.*), 138
Cullen, T. H. (for E. W. Riches), congenital hydronephrosis of unusual type (*By title*), 809
Cunliffe, A. C., modern methods in the control of airborne infections (*Disc.*), 383
curare, further experiences with (*Discussion*), 593
Currie, J. G. D., illumination (*Disc.*), 822
Curtis, F. R., venereal disease control in Denmark, Sweden and the British-occupied zone of Germany (*Disc.* on The present status of infectious disease control in continental Europe), 630

dacryocystorhinostomy (B. Reeves), 285
Dale, H. W. L., anæsthesia for abdomino-peritoneal operations for cancer of the *rectum* (*Disc.*), 269
  shock, with special reference to anæsthesia (*Disc.*), 178
Darier's disease and generalized pruritus (L. Forman), 8
Davenport, R. C. (*Disc.*), 818
  a family showing arachnodactyly with colobomata of lenses and choroid, 821
Davidson, M., birth control: some medical and legal aspects (*Disc.*), 51
Davies, O. V. Ll.-, see Lloyd-Davies, O. V.
Davies, W. W. W.-, see Wiggins-Davies, W. W.
Davis, D. R., disorders of skill: an experimental approach to some problems of neurosis, 583

Gabriel, W. B., a small high-grade carcinoma of the rectum with extensive lymphatic spread, 833
Ganado, W., the ætiology of chronic rheumatism (*Disc.*), 346
ganglia, basal, angioma of (L. J. Rowley), 164
Gardham, A. J., the diagnosis and treatment of tumours of the nasopharynx (*Disc.*), 711
Gardiner, P. (for T. K. Lyle), melanotic sarcoma (*By title*), 569
gastrectomy, transthoracic, for intussuscepted fibromyoma of fundus of stomach (N. C. Tanner), 275
    two cases (N. C. Tanner), 276
  with œsophagoduodenal anastomosis (A. D. Wright), 50
Gatman, M. (with C. H. Whittle and A. Lyell), Raynaud's phenomenon, with paroxysmal hæmoglobinuria, caused by cold agglutination, 500
Gauvain, Sir Henry, note on his contributions to orthopædic surgery (Sir T. Fairbank), 892
General Electric Company, two short films on illumination, 827
genito-urinary system, battle casualties involving (G. E. Parker), 804
Germany, health problems in (*Discussion*), 89
Gervis, W. H., osteo-arthritis of the trapeziometacarpal joint treated by excision of the trapezium, 492
Gibberd, G. F., the management of the normal third stage of labour and of hæmorrhage therein (*Disc.*), 375
Gillies, J., further experiences with curare (*Disc.*), 600
Gimblett, C. L., bilateral embolus of central retinal artery (*By title*), 569
Giri, D. V., the diagnosis and treatment of tumours of the nasopharynx (*Disc.*), 137
  illumination (*Disc.*), 828
glandular tumours of dog (E. Cotchin), 636
Glass, E. J. G., anterior ethmoidal hæmorrhage (*Disc.*), 283
Glover, J. A., otology in school children and child welfare (*Disc.*), 108
  whooping cough and measles: an epidemiological concurrence and contrast (*Disc.*), 398
Godtfredsen, E., ophthalmo-neurological symptoms in malignant nasopharyngeal tumours, 131, 138
goitre, exophthalmic (J. M. Alexander), 546
  toxic, treatment of (*Discussion*), 609
Goldman, V., anæsthesia for abdomino-peritoneal operations for cancer of the rectum (*Disc.*), 269
Goldsmith, W. N. (*Disc.*), 261, 706
  erythematous initial tuberculide (*Disc.*), 257
  hyperkeratotic systematized nævus with ? bromide eruption, see Hargreaves, A.
Gomme, R. E., analysis of function (*Disc.*), 300
Gordon, H. W. (*Disc.*), 704
  mycosis fungoides, 700
  Pringle's disease (adenoma sebaceum), 700
Graham, J. M., and McWhirter, R., carcinoma of the thyroid, 669
granulosis rubra nasi (D. I. Williams), 499
Gray, C., further experiences with curare (*Disc.*), 601
Greece, malaria control with D.D.T. (J. M. Vine), 841
Green, B., lupus vulgaris and tuberculides of face, 253
  mycosis fungoides, 504
  mycosis fungoides—treated with thorium X, 503
  and Freudenthal, W.; myxœdema papulosum, 702
  and McKean, C. W. F., sarcoidosis, 704
Green, H. N., shock, with special reference to anæsthesia (*Disc.*), 167, 178
Green, T. A., the treatment of cancer of the tongue (*Disc.*), 418
Green-Armytage, V. B., birth control: some medical and legal aspects (*Disc.*), 57
Greenfield, J. G. (*Disc.*), 554
  cerebral œdema (*Disc.*), 695
Greenland Eskimos, dental investigations (P. O. Pedersen), 726
Greeves, R. A., radiotherapy in the treatment of non-malignant superficial eye lesions (*Disc.*), 570
Greville, G. D., and Last, S. L., electroencephalographic studies (*Disc.* on Leucotomy as an instrument of research), 145
Griffith, E. F., birth control; some medical and legal aspects (*Disc.*), 58
Griffiths, H. E., analysis of function, 293
Griffiths, I. H. (for E. W. Riches), congenital hydronephrosis in a child aged 4½ years (*By title*), 809
Grüneberg, H., inherited disorders of the blood in rodents, 191
Guiot, G., cerebral œdema (*Disc.*), 689
Gunn, A. R.-, see Rugg-Gunn, A.
Gunn, W., modern methods in the control of airborne infections (*Disc.*), 383
Guttmann, L., the treatment and prognosis of traumatic paraplegia (*Disc.*), 219

Haddow, A. (with M. Mandeville), melanoma occurring in the viviparous fish *Heterandria formosa* and associated with sex reversal (*By title*), 638
hæmangioma, intracranial, causing convulsions (M. W. West), 164
hæmatology, comparative (H. H. Holman), 185
Hæmophilus influenzæ, relation to epidemic influenza (A. B. Rosher), 749
hæmorrhage, anterior ethmoidal (R. G. Macbeth), 280
  in third stage of labour, management of (*Discussion*), 370
Hall, D. W., otology in school children and child welfare (*Disc.*), 107
Hall, I. S., review of surgery of otosclerosis (*Disc.*), 327
  transmeatal attico-antrotomy in chronic tympanomastoid suppuration (*Disc.*), 771
Halton, J., further experiences with curare (*Disc.*), 601
Hamblen-Thomas, C., review of surgery of otosclerosis (*Disc.*), 328

epistaxis (J. Collier), 277
  (R. G. Macbeth), 280
erythema induratum (H. W. Barber), 245
  multiforme (C. H. Whittle), 701
erythroblastosis fœtalis (L. K. Diamond), 546
erythrodermia, congenital ichthyosiform (I. M. Scott), 701
  exfoliative (J. E. M. Wigley), 246
  leukæmic (G. B. Mitchell-Heggs, H. Corsi, and K. D. Crow), 249
Eskimos, dental investigations (P. O. Pedersen), 726
Europe, infectious disease control in (*Discussion*), 623
Evans, F. T., anæsthesia for abdomino-peritoneal operations for cancer of the rectum (*Disc.*), 266, 270
Evans, G., the management of patients with essential hypertension (*Disc.*), 773
Evans, P., hepatosplenomegaly: for diagnosis, see Saunders, C. F.
  oxycephaly, 166
Everidge, J., injuries of the urethra (*Disc.*), 806
  injuries to the bladder (*Disc.*), 806
eye, see also intra-ocular . . .
  effect of X-radiation on, clinical aspects (M. E. Cripps), 109
  lesions, non-malignant superficial, radiotherapy in (*Discussion*), 570
Eysenck, H. J., the measurement of personality, 75

face, unilateral hypoplasia (E. C. Sprawson), 835
facial bones, osteitis fibrosa affecting (M. A. Rushton), 316
  "three-ply" structure (W. W. James), 511
Fairbank, Sir Thomas, brief note on the contributions of the late Sir Henry Gauvain to orthopædic surgery, 892
Fairfield, L., birth control: some medical and legal aspects (*Disc.*), 58
favus (E. C. Jones), 506
Feeny, P. J. (*Disc.*), 10, 11, 504, 701, 706
Feiwel, M. (with G. B. Mitchell-Heggs), pityriasis rubra pilaris, 479
Felix, E., allergy in ophthalmology (*Disc.*), 581
femur, cyst in (G. O. Tippett), 485
  neck of, fractures, trifin nail in treatment (G. K. McKee), 236
fenestration operation for otosclerosis (E. R. G. Passe), 319
  microscope for (J. F. Simpson), 320
  technique (E. R. G. Passe), 319
Fergusson, J. D., ligation of the inferior vena cava for femoral thrombosis with pulmonary infarction, 49
? fibrosarcoma of abdominal wall (A. C. Roxburgh), 259
finger, osteomyelitis, X-ray treatment (A. H. Baker), 111
Finzi, N. S., radiotherapy in the treatment of non-malignant superficial eye lesions (*Disc.*), 577
  X-ray treatment of inflammatory diseases (*Disc.*), 115
fistula, arteriovenous, non-traumatic (C. G. Rob), 470
Fitzgerald, F. P., treatment of displacement of the radio-ulnar joint, 488
Flack, I. H., the pre-history of midwifery, 713
Fleming, J. A. C., large chronic rodent ulcer treated by radiotherapy, 469
Fletcher, C. M., the present position in regard to the pneumoconioses (*Disc.*), 783
Fletcher, E., the ætiology of chronic rheumatism (*Disc.*), 345
Flett, R. L., transmeatal attico-antrotomy in chronic tympanomastoid suppuration (*Disc.*), 771
Flew, J. D. S., the management of the normal third stage of labour and of hæmorrhage therein (*Disc.*), 370
Florey, Lady, the use of penicillin in urology (*Disc.*), 440
fluids, body, sudden shifts in (G. R. Cameron), 1
folklore, obstetrical (I. H. Flack), 713
Folley, S. J., recent researches on the physiology of mammary development and function (*Disc.* on Some recent developments in knowledge of the physiology of the breast), 903
Ford, E. B., the genetic aspects of birth control (*Disc.* on Birth control: some medical and legal aspects), 51
Forgan, R., the treatment of syphilis with penicillin (*Disc.*), 816
Forman, L. (*Disc.*), 9, 248, 701
  acne conglobata, 699
  Darier's disease and generalized pruritus, 8
  papulo-necrotic tuberculides, 248
Forrester, A. C., further experiences with curare (*Disc.*), 600
Forster, H. V. (*Disc.*), 285
  anterior ethmoidal hæmorrhage (*Disc.*), 282
  otology in school children and child welfare (*Pres. address*), 101, 108
  review of surgery of otosclerosis (*Disc.*), 328
  transmeatal attico-antrotomy in chronic tympanomastoid suppuration (*Disc.*), 772
Forty, F., associated carcinoma of colon and rectum: report of two cases, 872
Foulds, L., teratomas and mixed tumours in animals and their bearings on human pathology (*Disc.*), 635
fracture, Monteggia (W. S. Creer), 241
Franceschetti, A., toxoplasmosis: two cases, 821
Fraser, I. T., full-term intraligamentary pregnancy, 378
Freshman, E., the use of penicillin in urology (*Disc.*), 442
Freudenthal, W. (*Disc.*), 13, 481, 700, 701
  myxœdema circumscriptum (histological demonstration of Dr. Brian Russell's case for diagnosis, *Proc. R. Soc. Med.*, 40, 12), 258
  (with B. Green), myxœdema papulosum, 702
Freund, F., X-ray treatment of inflammatory diseases (*Disc.*), 113
Fulton, F. (with C. H. Andrewes, W. H. Bradley and D. K. M. Chalmers), common cold: interim report on a transmission experiment, 632
function, analysis of (H. E. Griffiths), 293
fundus, peripheral cystic degeneration (J. G. Milner), 820

intra-ocular foreign body, non-magnetic (P. McG. Moffatt), 817
  neoplasm, secondary (P. McG. Moffatt), 818
intussusception of fibromyoma of fundus of stomach, gastrectomy for (N. C. Tanner), 275
Ironside, R. N. (*Disc.*), 87

James, N. R., premedication (*Disc.* on Local analgesia), 525
James, U., juvenile cirrhosis, 162
  lipodystrophy, see MacGregor, M. E.
James, W. W., the "three-ply" structure in facial bones, 511
Janus, F., gross euphoria, corrected surgically (*By title*), 432
  neuroretinitis of undetermined ætiology (*By title*), 432
Jarman, R., anæsthesia for abdomino-perineal operations for cancer of the rectum (*Disc.*), 263
jaundice, acholuric, Paterson-Plummer-Vinson syndrome (L. Rau), 271
Jaworski, J., anterior poliomyelitis (*Disc.*), 932
Jefferson, G., cerebral œdema (*Disc.*), 694
  isolated oculomotor palsy caused by intracranial aneurysm, 419
Jobson, T. B., anterior ethmoidal hæmorrhage (*Disc.*), 283
Jonason, P. H. A., the treatment and prognosis of traumatic paraplegia (*Disc.*), 230
Jones, D. S., see Stanley-Jones, D.
Jones, E. C., favus, 506
  leukæmia cutis: ? myeloid leukæmia, 483
  ? lupus vulgaris, 506
  Senear-Usher syndrome, 705
Jones, E. I., myelosclerosis with leukæmoid blood picture, 117
Joshua, J. O., some glandular tumours of the dog (*Disc.*), 638

kala-azar in infancy (J. E. Debono), 155
? Kaposi's varicelliform eruption (C. H. Whittle), 252
Kelleher, W. H., anterior poliomyelitis (*Disc.*), 931
Kennedy, A., birth control: some medical and legal aspects (*Disc.*), 58
Kennedy, T. F., health problems in Germany (*Disc.*), 89
keratoderma palmaris et plantaris (G. C. Wells), 9
Kerley, P., disseminated ossified nodules in the lungs associated with mitral stenosis (*Disc.*), 408
  value of tomography in lesions of the main bronchi and their larger sub-divisions (*Disc.*), 404
Kersley, G. D., the ætiology of chronic rheumatism (*Disc.*), 343
Kidd, H. A., an aid to swallowing after laryngo-pharyngectomy for post-cricoid carcinoma, 284
kidney lesions due to dietary deficiencies (H. Heller and S. E. Dicker), 351
Kilner, T. P., cases and case records illustrating orthopædic and plastic surgical team work, 892
Kilpatrick, F. R., hydatids of the bladder (*By title*), 433
  hydatids of the kidney (*By title*), 433
  hydatids passed in micturition (*By title*), 433
King, A. J., the treatment of syphilis with penicillin (*Disc.*), 815
King, R. A., complete rupture of right quadriceps and partial rupture of left quadriceps tendons (*By title*), 293
  ? rheumatoid arthritis and ankylosing spondylitis (*By title*), 433
  spontaneous forward subluxation of atlas on axis (*By title*), 293
  tendon transplantation for posterior interosseous nerve paralysis, 272
Kingsley-Pillers, E. M. (for R. Dobbs), hyperelasticity of skin, 537
Kirk, J., congenital anomalies of the anorectal region (*Disc.*), 876
Kirk, J. B., the present status of infectious disease control in continental Europe (*Disc.*), 631
Knight, G. C. (*Disc.*), 83
Kon, S. K., and Mawson, E. H., studies of certain vitamins and other constituents of human milk (*Disc.* on Some recent developments in knowledge of the physiology of the breast), 900
Korenchevsky, V., the span of life (*Disc.*), 643
Korvin, H. G., pseudocoxalgia: (Calvé-Legg-Perthes' disease) the radiographic changes outside the femoral head, 886
Kremer, M., temporal arteritis, 84
Kyrle's disease (J. R. Simpson), 262

labour, third stage, management of (*Discussion*), 370
lactation, physiology (*Discussion*), 899
Langston, H. H., the Brittain method of arthrodesis of the hip, 895
laryngo-pharyngectomy, aid to swallowing after (H. A. Kidd), 284
laryngoscope, indirect, preliminary model (W. O. Lodge), 286
larynx, cancer of, review of series of cases (V. E. Negus), 515
  paralysis, anatomical and pathological considerations (V. E. Negus), 849
  recurrent papillomata and webbing of (D. F. A. Neilson), 286
Last, S. L. (with G. D. Greville), electroencephalographic studies (*Disc.* on Leucotomy as an instrument of research), 145
Laurent, L. J. M., acute meningo-encephalitis of undetermined virus ætiology, 927
Law, F. W., ring scotoma after retrobulbar neuritis, 138
Le Beau, J., cerebral œdema (*Disc.*), 689
Lederman, M., radiotherapy in the treatment of non-malignant superficial eye lesions (*Disc.*), 573, 577
  and Rugg-Gunn, A., Mooren's ulcer (*By title*), 569

Hammond, J., the span of life (*Disc.*), 641
Hankey, G. T., three cysts in the same mandible, not of dental origin: ? solitary cysts or osteitis fibrosa, 723
Hanley, H. G., actinomycosis of testicle (*By title*), 810
  a hazard of uretero-intestinal anastomosis (*By title*), 433
  retroperitoneal fibrosarcoma completely enveloping the kidney (*By title*), 433
  true hypernephroma of adrenal origin (*By title*), 810
  unusual ruptured kidney (*By title*), 433
Harbord, R. P., shock, with special reference to anæsthesia (*Disc.*), 172, 178
Hardman, J., treatment of cerebral abscess (*By title*), 884
Hare, R., modern methods in the control of airborne infections (*Disc.*), 383
Hargreaves, A. (for W. N. Goldsmith), hyperkeratotic systematized nævus with ? bromide eruption, 477
Harley, D., allergy in ophthalmology (*Disc.*), 582
Harnett, W. L., the treatment of cancer of the tongue (*Disc.*), 417
Harper, R. K., value of tomography in lesions of the main bronchi and their larger subdivisions (*Disc.*), 405
Harris, W. (*Disc.*), 83
  pain in the upper limb, excluding shoulder lesions (*Disc.*), 492
Hartley, J. B., value of tomography in lesions of the main bronchi and their larger subdivisions (*Disc.*), 404
Harvey, W., LeMay, C. H., and Shuttleworth, C. W., the sterilization of dental handpieces, 507
Harwood, F. C., modern methods in the control of airborne infections (*Disc.*), 382
health problems in Germany (*Discussion*), 89
Heber, J. (for H. M. M. Mackay), pneumatocele occurring during pneumonia and rupturing to form a pneumothorax, 534
  (for M. Wilmers), congenital syphilis, 161
Heggs, G. B. M.-, see Mitchell-Heggs, G. B.
Heller, H., and Dicker, S. E., some renal effects of experimental dietary deficiencies, 351
Hellier, F. F. (*Disc.*), 10, 14, 504
hemicolectomy, right (E. G. Muir), 831
hepatic flexure of colon, carcinoma (R. W. Raven), 876
hepatolenticular degeneration (D. H. Brinton), 556
hepatosplenomegaly (C. F. Saunders), 163
  (J. P. M. Tizard), 538
Hewitt, M., analysis of function (*Disc.*), 300
high-frequency currents, complex behaviour of, in simple circuits (P. Bauwens), 741
Himsworth, H. P., protein metabolism in relation to disease (*Pres. address*), 27
  radioactive tracers (*Disc.*), 360
Hindenach, J. C. R., tuberculous abscess formation following penicillin therapy, see Coope, P. J.
Hine, M. L. (*Disc.*), 820
  Coats's disease, 818
  retinitis proliferans, 818
hip, arthrodesis, Brittain method (H. H. Langston), 895
  osteo-arthritis, injection treatment (H. W. Crowe), 486
  tuberculosis, osteotomy for (M. C. Wilkinson), 238
Hobbs, H. E., megalocornea, 569
Hodgkin's disease (*Discussion*), 617
Hohmann, W. J. (*Disc.*), 262
  erythematous initial tuberculide, 255
Holinger, P. H., bronchial neoplasms (shown by G. H. Bateman) (*Film*), 858
Hollins, A. S. (*Disc.*), 556
Holman, H. H., studies on the hæmatology of the horse, ox and sheep, 185
homosexuality, social aspects of (*Discussion*), 585
Horsburgh, P. G., Berlin at the time of occupation (*Disc.* on Health problems in Germany), 93
horse, hæmatology of (H. H. Holman), 185
Howitt, F., analysis of function (*Disc.*), 300
Hudson, R. V., the treatment of acute peritonitis (*Disc.*), 128
  the treatment of toxic goitre (*Disc.*), 615
Huggett, A. St. G., radioactive tracers (*Disc.*), 360
Hughes, H. L., bilateral coloboma of the optic disc (introduced by A. Sorsby), 821
Humphreys, Sir Travers, birth control: some medical and legal aspects (*Disc.*), 57
Hunt, A., advanced carcinoma of the bladder excised by perineo-abdominal cystectomy (hydronephrosis and pyonephrosis) (shown by S. O. Aylett) (*By title*), 810
Hyde Memorial Lecture (H. Cohen), 443
hydronephrosis associated with abnormal vessels, treatment (H. H. Stewart), 807
hyperkeratosis follicularis et parafollicularis in cutem penetrans (J. R. Simpson), 262
hypertension, essential, management of (*Discussion*), 773
hypopituitarism (R. S. B. Pearson), 153
  long-standing, with recent signs suggesting chromophilic adenoma or suprasellar tumour (H. S. Le Marquand), 152
hypothyroidism with macular abiotrophy and inner ear deafness (L. Rau), 468

illumination (*Discussion*), 822
impetigo herpetiformis (J. E. M. Wigley), 248
incontinence in micturition, stress (*Discussion*), 361
infantilism, pituitary, with toxic goitre (A. W. Spence), 151
infectious disease control in continental Europe, present state of (*Discussion*), 623
inflammatory diseases, X-ray treatment (*Discussion*), 109
influenza, epidemic, relation of *Hæmophilus influenzæ* to (A. B. Rosher), 749
  laboratory diagnosis (J. A. Dudgeon), 660
Ingram, J. T. (*Disc.*), 245
  allergy in ophthalmology (*Disc.*), 579, 582
interosseous nerve paralysis, tendon transplantation for (R. A. King), 272
intervertebral discs, protrusion (R. H. Young), 233
intestine, small, carcinoid tumour associated with carcinoma of cæcum (C. N. Morgan), 874

MacCallum, F. O., anterior poliomyelitis (*Disc.*), 931
the laboratory diagnosis of virus infections (*Disc.*), 665
McCay, A. W., osteoma of nasopharynx, 286
McFadyean, K., birth control: some medical and legal aspects (*Disc.*), 55
McFarlane, A. S., radioactive tracers (*Disc.*), 354, 360
MacGregor, M. E. (for U. James), lipodystrophy, 533
McGuckin, F., otology in school children and child welfare (*Disc.*), 106
Mackay, H. M. M., congenital defect of the scalp, see Yudkin, S.
pneumatocele occurring during pneumonia and rupturing to form a pneumothorax, see Heber, J.
McKean, C. W. F., epidermolysis bullosa dystrophica, 705
(with B. Green), sarcoidosis, 704
McKee, G. K., the crossed trifin nail and graft in the treatment of fractures of the neck of the femur, 236
MacKeith, R. C. (with J. M. Watson), diagnosis of threadworms (*Demonst.*), 539
MacKenna, R. M. B. (*Disc.*), 502, 505
and Russell, B. F., cutaneous papillomatosis, 254
McKissock, W., angioma of the basal ganglia, see Rowley, L. J.
Mackwood, J. C., the social aspects of homosexuality (*Disc.*), 591
McLardy, T. (with A. Meyer), neuropathological studies (*Disc.* on Leucotomy as an instrument of research), 141
MacNalty, Sir Arthur S., the evolution of preventive medicine in England (*Pres. address*), 59
MacPhail, W. M., rehabilitation in chest injury (*Disc.*), 291
macular degeneration, familial, adolescent type (P. McG. Moffatt), 818
McWhirter, R. (with J. M. Graham), carcinoma of the thyroid, 669
Magill, I. W., anæsthesia in children (*Disc.*), 544
malaria control with D.D.T. (J. M. Vine), 841
Malkin, H. J., anæsthesia for Cæsarean section (*Disc.*), 568
Mallinson, F. B., further experiences with curare (*Disc.*), 598, 602
mammary physiology (*Discussion*), 899
Mandeville, M., and Haddow, A., melanoma occurring in the viviparous fish *Heterandria formosa* and associated with sex reversal (*By title*), 638
mandible, cysts of, non-dental (G. T. Hankey), 723
infections, severe (D. G. Walker), 309
Mannheim, H., the social aspects of homosexuality (*Disc.*), 587
Marre, I. R., effect of calciferol on lupus vulgaris (two cases), lupus pernio and Boeck's sarcoid, 10
Marshall, C. McI., anæsthesia for Cæsarean section (*Disc.*), 560
Martin, J. P. (*Disc.*), 553, 555, 556
mastoid and tympanic suppuration, attico-antrotomy in (A. Tumarkin), 761
Matthews, D. N., technique and value of tattooing in plastic surgery, 881
Mawson, E. H. (with S. K. Kon), studies of certain vitamins and other constituents of human milk (*Disc.* on Some recent developments in knowledge of the physiology of the breast), 900
Maxwell, J. P., osteomalacia, 738
May, W. R. (with G. B. Mitchell-Heggs), pili torti, 481
Meadows, S. P., papillœdema associated with chronic bronchitis, emphysema and polycythæmia, 555
spontaneous carotid-cavernous aneurysm, 554
measles and whooping cough, epidemiological concurrence and contrast (W. Butler), 384
median nerve, compression neuritis of (W. R. Brain and A. D. Wright), 83
Medical Society for the Study of Venereal Diseases, joint meeting with Section of Experimental Medicine and Therapeutics, 811
medicine, clinical, history of (A. P. Cawadias), 453
Medvei, V. C., pituitary infantilism with toxic goitre (*Disc.*), 152
megalocornea (H. E. Hobbs), 569
meningitis, treatment with penicillin (H. V. Smith), 681
meningo-encephalitis, acute, of undetermined virus ætiology (L. J. M. Laurent), 927
Merewether, E. R. A., the present position in regard to the pneumoconioses' (*Disc.*), 781
metabolism, protein, in relation to disease (H. P. Himsworth), 27
Meyer, A., and McLardy, T., neuropathological studies (*Disc.* on Leucotomy as an instrument of research), 141
micturition, stress incontinence (*Discussion*), 361
midwifery, pre-history (I. H. Flack), 713
milk, human, vitamins and other constituents of (S. K. Kon and E. H. Mawson), 900
Mill, W. A., otology in school children and child welfare (*Disc.*), 108
Miller, F. J. W., prematurity in an industrial town (*By title*), 550
Miller, R. G., sclerosis of left sacro-iliac joint (*By title*), 293
Millin, T., stress incontinence in micturition (*Disc.*), 364
Milner, J. G., peripheral cystic degeneration: ? prognosis, 820
Mimpriss, T. W., neurofibroma of stomach in von Recklinghausen's disease, 120
malignant lympho-endothelioma of neck, 471
and Birt, St. J. M. C., bladder neck dysfunction (*By title*), 809
transurethral resection in a patient of 80 (*By title*), 809
tumour for diagnosis (*By title*), 809
two cases of imperfect descent of the testicle (*By title*), 809
unusual ulcer of the bladder (*By title*), 809
(with R. H. O. B. Robinson and W. W. Wiggins-Davies), carcinoma of the bladder treated by local operation (*By title*), 809
carcinoma of the prostate and carcinoma of the colon (*By title*), 809

Lee, H. G., dematitis bullosa striata pratensis (introduced by I. Muende), 14
leg, recurrent ulcers (G. C. Wells), 482
  thrombosis, pathology (R. H. D. Short), 195
leiomyoma cutis (G. B. Mitchell-Heggs and M. H. Small), 249
Le Marquand, H. S., long-standing hypopituitarism with recent signs suggesting either chromophilic adenoma or suprasellar tumour, 152
LeMay, C. H. (with W. Harvey and C. W. Shuttleworth), the sterilization of dental handpieces, 507
leontiasis ossea associated with Paget's disease (A. Elkeles), 466
leucoderma and leucotrichia (B. F. Russell), 506
leucotomy, prefrontal, as an instrument of research (*Discussion*), 141
leukæmia cutis (E. C. Jones), 483
  lymphatic, erythrodermia in (G. B. Mitchell-Heggs, H. Corsi and K. D. Crow), 249
  myeloid (E. C. Jones), 483
Le Vay, D., pain in the upper limb, excluding shoulder lesions (*Disc.*), 494
Levy, Harold (*Disc.*), 131, 140, 817, 820
  illumination (*Disc.*), 827, 828
Levy, Herbert (*Disc.*), 160, 272, 538
Lewis, I., leontiasis ossea, see Willcox, J. M.
  the packing of abdominal incisions in peritonitis, 652
  sarcoma of bronchus, 119
lichen nitidus (J. R. Simpson), 9
  planus hypertrophicus (C. H. Whittle), 7
    in boy of 8 (H. Corsi), 477
  sclerosus (H. J. Wallace), 8
lichenoid dermatitis, tropical (H. J. Wallace), 502
Lidwell, O. M., modern methods in the control of airborne infections (*Disc.*), 382
life, span of (*Discussion*), 638
light eruption (F. R. Bettley), 261
lighting, see illumination
Lightwood, R. C., intracranial hæmangioma causing convulsions, see West, M. W.
limb, upper, pain in (*Discussion*), 492
Lindgren, E., the normal temporal horn and its deformities by tumours in the middle cerebral fossa, 859
lipodystrophy (M. E. MacGregor), 533
Lister, A., (a) diabetic cataract; (b) endocrine cataract, 130
lithiasis, renal, problems (R. H. O. B. Robinson), 201
liver, cirrhosis, in child of 7 (U. James), 162
  disease, nutritional, in West Indian infants (J. C. Waterlow), 347
Lloyd, H. N., the management of the normal third stage of labour and of hæmorrhage therein (*Disc.*), 371
Lloyd, K. N., bilateral brachial neuralgia with osteo-arthritic changes of C.6 and C.7 (female) (*By title*), 293
  left brachial neuralgia following a fall: X-ray showed diminished disc space between C.5 and C.6 (male) (*By title*), 293
  left brachial neuralgia, with osteo-arthritic changes of C.6 and C.7 (male) (*By title*), 293
Lloyd-Davies, O. V., anæsthesia for abdomino-peritoneal operations for cancer of the rectum (*Disc.*), 268
  carcinoma of the rectum with a single secondary in the liver: synchronous combined incision and left hepatectomy, 875
Lloyd-Williams, K., anæsthesia for Cæsarean section (*Disc.*), 562
Lodge, T., disseminated ossified nodules in the lungs associated with mitral stenosis (*Disc.*), 408
  value of tomography in lesions of the main bronchi and their larger sub-divisions (*Disc.*), 405
Lodge, W. O., preliminary model for an indirect laryngoscope (*Exhibit*), 286
longevity (*Discussion*), 638
Lourie, E. M., the treatment of syphilis with penicillin (*Disc.*), 814
lues, see syphilis
lungs, collapse of lower lobes in children (N. C. Oswald), 736
  nodular calcification associated with mitral stenosis (A. Elkeles), 405
lupus pernio, treatment with calciferol (I. R. Marre), 10
  vulgaris (E. C. Jones), 506
    and tuberculides of face (B. Green), 253
    treatment with calciferol (I. R. Marre), 10
    with epithelioma and mutilations (G. B. Mitchell-Heggs and J. R. Owen), 484
Lyell, A. (with C. H. Whittle and M. Gatman), Raynaud's phenomenon, with paroxysmal hæmoglobinuria, caused by cold hæmagglutination, 500
Lyle, T. K., congenital palsy of right superior oblique with compensatory head posture (ocular torticollis), 819
  melanotic sarcoma (*By title*), see Gardiner, P.
  relative palsy of left superior rectus due to local orbital tumour, 818
  right superior oblique paralysis due to right fourth cerebral nerve palsy caused by head injury, 819
  thrombophlebitis retinæ, 818
lymphadenoma (L. Rau), 468
lymphadenopathies, treatment (*Discussion*), 617
lymphocytoma, miliary (F. R. Bettley), 13
lymphoma (E. Wolff), 820

McAlpine, D. (*Disc.*) 81, 84, 85, 88, 552, 554, 556
  cerebral œdema (*Disc.*), 688
  some observations on the 1947 outbreak of acute poliomyelitis (*Disc.* on Anterior poliomyelitis), 929
  the treatment and prognosis of traumatic paraplegia (*Disc.*), 232
  (with C. P. Wilson), glossopharyngeal neuralgia treated by trans-tonsillar section of the nerve, 82
Macbeth, R. G., anterior ethmoidal hæmorrhage, 280
  otology in school children and child welfare (*Disc.*), 107

MacCallum, F. O., anterior poliomyelitis (*Disc.*), 931
  the laboratory diagnosis of virus infections (*Disc.*), 665
McCay, A. W., osteoma of nasopharynx, 286
McFadyean, K., birth control: some medical and legal aspects (*Disc.*), 55
McFarlane, A. S., radioactive tracers (*Disc.*), 354, 360
MacGregor, M. E. (for U. James), lipodystrophy, 533
McGuckin, F., otology in school children and child welfare (*Disc.*), 106
Mackay, H. M. M., congenital defect of the scalp, see Yudkin, S.
  pneumatocele occurring during pneumonia and rupturing to form a pneumothorax, see Heber, J.
McKean, C. W. F., epidermolysis bullosa dystróphica, 705
  (with B. Green), sarcoidosis, 704
McKee, G. K., the crossed trifin nail and graft in the treatment of fractures of the neck of the femur, 236
MacKeith, R. C. (with J. M. Watson), diagnosis of threadworms (*Demonst.*), 539
MacKenna, R. M. B. (*Disc.*), 502, 505
  and Russell, B. F., cutaneous papillomatosis, 254
McKissock, W., angioma of the basal ganglia, see Rowley, L. J.
Mackwood, J. C., the social aspects of homosexuality (*Disc.*), 591
McLardy, T. (with A. Meyer), neuropathological studies (*Disc.* on Leucotomy as an instrument of research), 141
MacNalty, Sir Arthur S., the evolution of preventive medicine in England (*Pres. address*), 59
MacPhail, W. M., rehabilitation in chest injury (*Disc.*), 291
macular degeneration, familial, adolescent type (P. McG. Moffatt), 818
McWhirter, R. (with J. M. Graham), carcinoma of the thyroid, 669
Magill, I. W., anæsthesia in children (*Disc.*), 544
malaria control with D.D.T. (J. M. Vine), 841
Malkin, H. J., anæsthesia for Cæsarean section (*Disc.*), 568
Mallinson, F. B., further experiences with curare (*Disc.*), 598, 602
mammary physiology (*Discussion*), 899
Mandeville, M., and Haddow, A., melanoma occurring in the viviparous fish *Heterandria formosa* and associated with sex reversal (*By title*), 638
mandible, cysts of, non-dental (G. T. Hankey), 723
  infections, severe (D. G. Walker), 309
Mannheim, H., the social aspects of homosexuality (*Disc.*), 587
Marre, I. R., effect of calciferol on lupus vulgaris (two cases), lupus pernio and Boeck's sarcoid, 10
Marshall, C. McI., anæsthesia for Cæsarean section (*Disc.*), 560
Martin, J. P. (*Disc.*), 553, 555, 556
mastoid and tympanic suppuration, atticoantrotomy in (A. Tumarkin), 761
Matthews, D. N., technique and value of tattooing in plastic surgery, 881
Mawson, E. H. (with S. K. Kon), studies of certain vitamins and other constituents of human milk (*Disc.* on Some recent developments in knowledge of the physiology of the breast), 900
Maxwell, J. P., osteomalacia, 738
May, W. R. (with G. B. Mitchell-Heggs), pili torti, 481
Meadows, S. P., papillœdema associated with chronic bronchitis, emphysema and polycythæmia, 555
  spontaneous carotid-cavernous aneurysm, 554
measles and whooping cough, epidemiological concurrence and contrast (W. Butler), 384
median nerve, compression neuritis of (W. R. Brain and A. D. Wright), 83
Medical Society for the Study of Venereal Diseases, joint meeting with Section of Experimental Medicine and Therapeutics, 811
medicine, clinical, history of (A. P. Cawadias), 453
Medvei, V. C., pituitary infantilism with toxic goitre (*Disc.*), 152
megalocornea (H. E. Hobbs), 569
meningitis, treatment with penicillin (H. V. Smith), 681
meningo-encephalitis, acute, of undetermined virus ætiology (L. J. M. Laurent), 927
Merewether, E. R. A., the present position in regard to the pneumoconioses' (*Disc.*), 781
metabolism, protein, in relation to disease (H. P. Himsworth), 27
Meyer, A., and McLardy, T., neuropathological studies (*Disc.* on Leucotomy as an instrument of research), 141
micturition, stress incontinence (*Discussion*), 361
midwifery, pre-history (I. H. Flack), 713
milk, human, vitamins and other constituents of (S. K. Kon and E. H. Mawson), 900
Mill, W. A., otology in school children and child welfare (*Disc.*), 108
Miller, F. J. W., prematurity in an industrial town (*By title*), 550
Miller, R. G., sclerosis of left sacro-iliac joint (*By title*), 293
Millin, T., stress incontinence in micturition (*Disc.*), 364
Milner, J. G., peripheral cystic degeneration: ? prognosis, 820
Mimpriss, T. W., neurofibroma of stomach in von Recklinghausen's disease, 120
  malignant lympho-endothelioma of neck, 471
  and Birt, St. J. M. C., bladder neck dysfunction (*By title*), 809
   transurethral resection in a patient of 80 (*By title*), 809
   tumour for diagnosis (*By title*), 809
   two cases of imperfect descent of the testicle (*By title*), 809
   unusual ulcer of the bladder (*By title*), 809
  (with R. H. O. B. Robinson and W. W. Wiggins-Davies), carcinoma of the bladder treated by local operation (*By title*), 809
   carcinoma of the prostate and carcinoma of the colon (*By title*), 809

Mimpriss, T. W. (with R. H. O. B. Robinson and W. W. Wiggins-Davies), ectopic kidney with pyuria (*By title*), 809
  giant ureteric calculi (*By title*), 809
  hypernephroma (*By title*), 809
  intracapsular nephrectomy for recurrent renal calculi (*By title*), 809
  renal calculi (*By title*), 809
  transurethral resection in a man of 80 (*By title*), 809
  tuberculous kidney (*By title*), 809
  tuberculous kidney showing extensive calcification (*By title*), 809
  ureteric transplantation and cystectomy for carcinoma (*By title*), 809
  ureteric transplantation for obstetrical injury (*By title*), 809
Minnitt, R. J., shock, with special reference to anæsthesia (*Disc.*), 177
Mitchell-Heggs, G. B. (*Disc.*), 482
  ? poikiloderma: ? premycosis, 480
  Corsi, H., and Crow, K. D., erythrodermia in lymphatic leukæmia (malignant erythrodermia), 249
  and Feiwel, M., pityriasis rubra pilaris, 479
  and May, W. R., pili torti, 481
  and Owen, J. R., lupus vulgaris with epithelioma and mutilations, 484
  and Small, M. H., leiomyoma cutis, 249
Mitman, M., anterior poliomyelitis (*Disc.*), 932
  modern methods in the control of airborne infections (*Disc.*), 383
Mitra, S., the evaluation of the results of carcinoma of the cervix uteri treated by radical vaginal operation (*Disc.* on Some aspects of surgical and radiological treatment of carcinoma of the cervix), 907
mitral incompetence, retinal hæmorrhage with (N. Pines), 140
  stenosis, nodular calcification in lungs associated with (A. Elkeles), 405 (*bis*)
Moerch, E. T., controlled respiration by means of special automatic machines as used in Sweden and Denmark, 603
Moffatt, P. McG. (*Disc.*), 817
  familial macular degeneration: adolescent type, 818
  hole at the macula following trauma (*By title*), 818
  intra-ocular body, non-magnetic, 817
  intra-ocular secondary neoplasm, 818
Mogg, R. A., injuries to the bladder, 795, 807
Moir, J. C., stress incontinence in micturition (*Disc.*), 367
Molesworth, H. W. L., local analgesia (*Disc.*) 529
mongolian patch, blue nævus in (C. L. Collins), 505
Monkhouse, J. P., review of surgery of otosclerosis (*Disc.*), 328
Monteggia fracture (W. S. Creer), 241
Moore, J. E., the treatment of syphilis with penicillin (*Disc.*), 811, 816
Mooren's ulcer, radiotherapy (A. J. D. Smith), 576
Morgan, C. N., carcinoma of the cæcum associated with carcinoid tumour of the small intestine, 874
Morgan, O. G., allergy in ophthalmology (*Disc.*), 578, 582
Morley, J., the treatment of acute peritonitis (*Disc.*), 123
morphœa guttata (B. F. Russell), 506
? Morquio's disease (J. A. Cholmeley), 491
Morson, A. C., hydatid disease of the kidney (two cases) (*By title*), 433
  the use of penicillin in urology (*Disc.*), 441
Mountford, L. O., further experiences with curare (*Disc.*), 601
Muende, I., see Lee, H. G.
Muir, E. G., right hemicolectomy, 831
Murley, R. S., calcified left kidney with ureter and two dense calcified foci in the middle zone of the left lung (*By title*), 810
  pyelonephritis with multiple cortical abscess formation in a kidney with double pelvis and ureter (*By title*), 810
muscular dystrophy, pseudo-hypertrophic (J. M. Alexander), 546
mycosis fungoides (H. W. Gordon), 700
    (B. Green), 504
    (J. R. Owen), 505
    treated with thorium X (B. Green), 503
myelosclerosis with leukæmoid blood picture (E. I. Jones), 117
myoclonus (E. A. Carmichael), 553
myxœdema circumscriptum (W. Freudenthal), 258
    (B. F. Russell), 12
  papulosum (B. Green and W. Freudenthal), 702

Nabarro, D., the treatment of syphilis with penicillin (*Disc.*), 816
Nabarro, J. D. N., treatment of the adenopathies (*Disc.*), 622
nævus, systematized (A. Hargreaves), 477
nasal obstruction (T. M. Boyle), 283
nasopharynx, osteoma of (A. W. McCay), 286
  tumours, diagnosis and treatment (E. D. D. Davis), 135, 707
    ophthalmo-neurological symptoms in (E. Godtfredsen), 131
Nathan, P. W., the treatment and prognosis of traumatic paraplegia (*Disc.*), 232
neck, lympho-endothelioma (T. W. Mimpriss), 471
Negus, V. E., certain anatomical and physiological considerations in paralysis of the larynx, 849
  intrinsic cancer of the larynx: review of a series of cases, 515
  review of surgery of otosclerosis (*Disc.*), 327
Neilson, D. F. A., recurrent papillomata and webbing of the larynx, 286
nephritis with œdema (B. W. Powell), 544
neuralgia, glossopharyngeal, treated by transtonsillar section of the nerve (C. P. Wilson and D. McAlpine), 82
neuritis due to compression of median nerve (W. R. Brain and A. D. Wright), 83
  retrobulbar, ring scotoma after (F. W. Law), 138
neurofibromatosis (J. M. Alexander), 546
  multiple, bone deformity associated with (N. C. Tanner), 47
neurology, penicillin in (*Discussion*), 681
neuro-ophthalmological symptoms in malignant nasopharyngeal tumours (E. Godtfredsen), 131

neuropathological studies contributed by leucotomy (A. Meyer and T. McLardy), 141
neurosis, experimental approach (D. R. Davis), 583
Nevin, S. (with P. Collard), affection of the trigeminal nerve nucleus and central grey matter of the spinal cord following the administration of stilbamidine, 87
Nicol, W. D., and Whelen, M., penicillin and neurosyphilis (*Disc.* on Penicillin in neurology), 684
Nissen, K. I., degloving accident to left lower leg, treated by immediate full-thickness grafts obtained from the skin flaps (*By title*), 492
  degloving accident to right fore-arm, followed by necrosis of skin flaps, &c. (*By title*), 492
  poliomyelitis on St. Helena, 1945-6 (*Disc.* on Anterior poliomyelitis), 923
Noble, F. A. W.-, see Williamson-Noble, F. A.
nodular calcification in lungs associated with mitral stenosis (A. Elkeles), 405 (*bis*)
Norman, A. P. (for D. Paterson), calcinosis universalis, 160
  sclerema, 160
nose, epithelioma of, with destruction of nasal septum (H. S. Sharp), 284
nose-bleeding, see epistaxis
Nowell, S., value of tomography in lesions of the main bronchi and their larger subdivisions, 399
Nussey, A. M., the treatment of toxic goitre (*Disc.*), 614
nutritional liver disease in West Indian infants (J. C. Waterlow), 347
nystagmus, ataxic, in disseminated sclerosis (W. Harris), 81

Oakley, C. L., the constituents of normal human blood, 190
  teratomas and mixed tumours in animals and their bearings on human pathology (*Disc.*), 636
oblique inferior muscle, paralysis (A. S. Philps), 817
  superior muscle, paralysis, congenital, and compensatory head posture (T. K. Lyle), 819
    paralysis due to fourth cerebral nerve palsy caused by head injury (T. K. Lyle), 819
obstetrics, pre-history (I. H. Flack), 713
oculomotor nerve, paralysis caused by intracranial aneurysm (G. Jefferson), 419
O'Donovan, W. J. (*Disc.*), 11
œdema, cerebral (*Discussion*), 686
œsophagoduodenal anastomosis with gastrectomy (A. D. Wright), 50
œsophagus, carcinoma of, treated by resection and presternal œsophago-gastrectomy (H. Taylor), 465
  lesion associated with sclerodactylia (W. A. Bourne), 463
Ogilvie, A., treatment and prognosis of bronchiectasis (*By title*), 550
ophthalmology, allergy in (*Discussion*), 578
orbit, plastic implant into (F. A. Williamson-Noble), 130
Organe, G. S. W., further experiences with curare (*Disc.*), 596
orthopædic and plastic surgical team work (T. P. Kilner), 892
osteitis fibrosa, regional, of facial bones (M. A. Rushton), 316
  typhoid, of long bones (E. T. Bailey), 486
osteomalacia (J. P. Maxwell), 738
osteomyelitis of fingers, X-ray treatment (A. H. Baker), 111
osteoporosis circumscripta with Paget's disease and leontiasis ossea (A. Elkeles), 466
Oswald, N. C., collapse of the lower lobes of the lungs in children, 736
otology in school children (H. V. Forster), 101
otosclerosis, fenestration operation for (E. R. G. Passe), 319
  surgery of, review (T. Cawthorne), 320
Owen, J. R., mycosis fungoides, 505
  (with G. B. Mitchell-Heggs), lupus vulgaris with epithelioma and mutilations, 484
ox, hæmatology of (H. H. Holman), 185
oxycephaly (P. Evans), 166

Page, Sir Max, physiotherapy in an accident service, 15
Paget's disease in association with osteoporosis circumscripta and leontiasis ossea (A. Elkeles), 466
  of skull with platybasia (J. Bull), 85
pain in the upper limb excluding shoulder lesions (*Discussion*), 492
pan-hypopituitarism (R. S. B. Pearson), 153
papillœdema associated with chronic bronchitis, emphysema and polycythæmia (S. P. Meadows), 555
papilloma of rectum, difference from adenoma explained (C. E. Dukes), 829
papillomatosis, cutaneous (R. M. B. MacKenna and B. F. Russell), 254
paralysis, infantile, see poliomyelitis
paraplegia, traumatic, treatment and prognosis (*Discussion*), 219
paraplegic eunuch with lues (M. Critchley), 552
parapsoriasis, retiform variety (J. E. M. Wigley), 699
parathyroids, hyperplasia, in boy of 8 (N. F. E. Burrows), 154
Parker, G. E., carcinoma of the bladder: total cystectomy (*By title*), 809
  congenital bilateral hydronephrosis (*By title*), 809
  giant ureteric calculus (*By title*), 809
  some observations on a personal series of battle casualties involving the genito-urinary system, 804
Parkes, A. S., overactivity of the adrenal cortex (*Disc.*), 45
Parkinsonism, post-encephalic, with palilalia (M. Critchley), 552
paroophoron, carcinoma (A. L. Abel), 834
Passe, E. R. G., bilateral clinical otosclerosis treated by the fenestration operation using the cartilage stopple and the endaural approach, 319
  technique of fenestration operation, 319
Paterson, D., angioma of the basal ganglia, see Rowley, L. J.

Paterson, D., calcinosis universalis, see Norman, A. P.
  hepatosplenomegaly, see Tizard, J. P. M.
  sclerema, see Norman, A. P.
  staphylococcal pneumonia with obstructive emphysema, see Scott, L. G.
  the treatment of cancer of the tongue (*Disc.*), 412
Paterson-Plumer-Vinson syndrome in acholuric jaundice (L. Rau), 271
Patterson, J., overactivity of the adrenal cortex (*Disc.*), 46
Patterson, N. (*Disc.*), 284, 285, 286
  the treatment of subacute maxillary sinusitis, especially in children (*Disc.*), 857
Paul, J. W. (for S. Yudkin), spontaneous bilateral pneumothorax occurring in a premature baby during the neo-natal period, 165
Pearson, R. S. B., pan-hypopituitarism, 153
Pedersen, P. O., dental investigations of Greenland Eskimos, 726
Peel, J. H., anæsthesia for Cæsarean section (*Disc.*), 559
Peeney, A. L. P., the use of penicillin in urology (*Disc.*), 433
pemphigus erythematosus (E. C. Jones), 705
  of pharynx (H. S. Sharp), 284
  vegetans (J. E. M. Wigley), 248
penicillin concentration in bile (E. G. Tuckwell), 654
  in neurology (*Discussion*), 681
  in treatment of syphilis (*Discussion*), 811
  in urology (*Discussion*), 433
  therapy, tuberculous abscess following (P. J. Coope), 161
Penman, G. G., choroidal neoplasm, 819
  dermoid cyst, simulating neoplasm of lacrimal gland, 820
  Eales' disease (*By title*), 819
Penrose, L. S., the importance of statistics in psychiatry, 863
periostitis, traumatic (R. M. Todd), 535
peritonitis, acute, treatment (*Discussion*), 123
  packing of abdominal incisions in (I. Lewis), 652
personality, measurement (H. J. Eysenck), 75
  morphological level (J. M. Tanner), 301
Petch, C. P. (for O. L. V. de Wesselow), xanthomatosis, 118
pharynx, pemphigus of (H. S. Sharp), 284
Philipp, E., the treatment of tuberculous salpingitis with special reference to X-ray therapy, 376
Philps, A. S., asthma, eczema, cataract, 817
  Devicz's disease (*By title*), 569
  palsy of L. inferior oblique muscle, 817
  retinitis proliferans, 817
  tuberculous choroiditis, 817
physical functional analysis (H. E. Griffiths), 293
physiotherapy in an accident service (Sir M. Page), 15
physique, classification of (J. M. Tanner), 301
Piercy, J. E., the treatment of toxic goitre (*Disc.*), 609
pili torti (G. B. Mitchell-Heggs and W. R. May), 481
Pillers, E. M. K.-, see Kingsley-Pillers, E. M.
Pines, N. (*Disc.*), 139
  Denig's operation for trachoma: two cases, 129
Pines, N., Denig's operation for trachoma (two cases) (*By title*), 569
  Denig's operation: two cases, 139
  retinal hæmorrhage with mitral incompetence, 140
pityriasis rubra pilaris (G. B. Mitchell-Heggs), 479
platybasia complicating Paget's disease of the skull (J. Bull), 85
pneumatocele rupturing to form a pneumothorax (J. Heber), 534
pneumoconioses, present position in regard to (*Discussion*), 781
pneumonia, staphylococcal, with obstructive emphysema (L. G. Scott), 165
pneumothorax due to ruptured pneumatocele (J. Heber), 534
  spontaneous bilateral, in premature baby during neo-natal period (J. W. Paul), 165
Pochin, E. E., radioactive tracers (*Disc.*), 357
poikiloderma (G. B. Mitchell-Heggs), 480
  congenitale (C. H. Whittle), 499
poliomyelitis, anterior (*Discussion*), 923
  limited to trigeminal motor nuclei (D. J. Williams), 555
  1947 outbreak (D. McAlpine), 929
  on St. Helena (K. I. Nissen), 923
polycythæmia and papillœdema associated with bronchitis and emphysema (S. P. Meadows), 555
polypus, gastric, intussuscepted, gastrectomy for (N. C. Tanner), 275
Poole-Wilson, D. S., injuries of the urethra, 798
Powell, B. W. (for B. E. Schlesinger), diabetes insipidus, 544
  nephritis with œdema, 544
pregnancy, intraligamentary, full-term (I. T. Fraser), 378
premedication (N. R. James), 525
? premycosis (G. B. Mitchell-Heggs), 480
Prescott, F., the chemistry and pharmacology of local analgesic drugs (*Disc.* on Local analgesia), 527
  further experiences with curare (*in absentia* read by R. H. Roberts) (*Disc.*), 593
preventive medicine, evolution in England (Sir A. S. MacNalty), 59
Priddis, K. W. (for A. Small), cirsoid aneurysm, 121
Pringle's disease (H. W. Gordon), 700
proctology past and present (A. H. Whyte), 179
protein balance in acute peritonitis (C. G. Rob), 126
  metabolism in relation to disease (H. P. Himsworth), 27
proteins, serum, of domestic animals (J. B. Brooksby), 187
pruritus, generalized, and Darier's disease (L. Forman), 8
pseudocoxalgia (H. G. Korvin), 886
psychiatry, statistics in, importance of (L. S. Penrose), 863
puberty, precocious, ? of suprarenal origin (N. F. E. Burrows), 154
Purdie, A. W., birth control: some medical and legal aspects (*Disc.*), 57
pyoderma due to chronic ulcerative colitis, specimen of colon removed (R. S. Corbett), 871

radioactive tracers (*Discussion*), 354
radiotherapy in the treatment of non-malignant superficial eye lesions (*Discussion*), 570
radio-ulnar joint, displacement, treatment (F. P. Fitzgerald), 488
Raeburn, H. A., health problems in Germany (*Disc.*), 97
Ransom, S. G., local analgesia (*Disc.*), 531
Rau, L., hypothyroidism with macular abiotrophy and inner ear deafness, 468
  lymphadenoma, 468
  Paterson-Plummer-Vinson syndrome in a case of familial acholuric jaundice, 271
Raven, R. W., partial hepatectomy and right hemicolectomy for carcinoma of the hepatic flexure of the colon, 876
Raynaud's phenomenon, caused by cold hæmagglutination (C. H. Whittle, A. Lyell and M. Gatman), 500
Rea, R. L., penicillin and sulphonamides as a means of arresting cavernous sinus thrombosis in a case of pneumonia complicated with ophthalmic symptoms (*By title*), 582
Read, C. D., some aspects of surgical and radiological treatment of carcinoma of the cervix (*Disc.*), 909
Recklinghausen's disease (A. D. Wright), 49
  neurofibroma of stomach in (T. W. Mimpriss), 120
rectum and anus, congenital anomalies (*Discussion*), 876
  and colon, carcinoma of (F. Forty), 872
  cancer of, anæsthesia for abdomino-perineal operations (*Discussion*), 263
  carcinoma invading from paroophoron (A. L. Abel), 834
  carcinoma with extensive lymphatic spread (W. B. Gabriel), 833
  carcinoma with single secondary in liver (O. V. Lloyd-Davies), 875
  papilloma and adenoma, difference between (C. E. Dukes), 829
rectus superior muscle, paralysis due to orbital tumour (T. K. Lyle), 818
Reed, H. (for A. Sorsby), persistent pupillary membrane showing a network pattern (*By title*), 569
Reeves, B., persistent epiphora following dacrocystitis, 285
rehabilitation in chest injury (*Discussion*), 287
Reid, W. O., transmeatal attico-antrotomy in chronic tympanomastoid suppuration (*Disc.*), 772
Reitman, F., leucotomy as an instrument of research (*Disc.*), 147
Renwick, G., Krukenberg's spindle (*By title*), 432
  phakomatosis (*By title*), 432
  pseudoglioma (*By title*), 432
  ptosis with pseudo-Graefe phenomenon (*By title*), 432
respiration, control by special automatic machines (E. T. Moerch), 603
? reticulosis (B. F. Russell), 12
retina, detachment, ? treatment (E. Wolff), 820
  hæmorrhage, with mitral incompetence (N. Pines), 140
retinitis proliferans (M. L. Hine), 818
  (A. S. Philps), 817
Rewell, R. E., blood constituents of animals (*Disc.*), 192
  the span of life (*Disc.*), 644
rheumatic diseases, challenge and opportunity (H. Cohen), 443
rheumatism, chronic, ætiology of (*Discussion*), 329
Richards, G. E., the radiological treatment of carcinoma of the cervix uteri (*Disc.* on Some aspects of surgical and radiological treatment of carinoma of the cervix), 911
Riches, E. W., congenital hydronephrosis in a child aged 4½ years (*By. title*), see Griffiths, I. H.
  congenital hydronenhrosis of unusual type (*By title*), see Cullen, T. H.
  kidney with triple pelvis and large ureteric calculus (*By title*), 809
  squamous metaplasia in papillary carcinoma of the kidney (*By title*), 433
  the treatment and prognosis of traumatic paraplegia (*Disc.*), 225, 232
Rob, C. G., arteriovenous fistula without a history of trauma, 470
  protein balance in acute peritonitis (*Disc.* on The treatment of acute peritonitis), 126
Roberts, F. W., local analgesia (*Disc.*), 531
Robertson, M., the span of life (*Disc.*), 643
Robinson, R. H. O. B., some problems of renal lithiasis (*Pres. address*), 201
  (with T. W. Mimpriss and W. W. Wiggins-Davies), carinoma of the bladder treated by local operation (*By title*), 809
    carcinoma of the prostate and carcinoma of the colon (*By title*), 809
    ectopic kidney with pyuria (*By title*), 809
    giant ureteric calculi (*By title*), 809
    hypernephroma (*By title*), 809
    intracapsular nephrectomy for recurrent renal calculi (*By title*), 809
    renal calculi (*By title*), 809
    transurethral resection in a man of 80 (*By title*), 809
    tuberculous kidney (*By title*), 809
    tuberculous kidney showing extensive calcification (*By title*), 809
    ureteric transplantation and cystectomy for carcinoma (*By title*), 809
    ureteric transplantation for obstetrical injury (*By title*), 809
rodents, blood disorders, inherited (H. Grüneberg), 191
Romanes, G., the treatment and prognosis of traumatic paraplegia (*Disc.*), 232
Romano-British skulls from Compton burial-ground (Sir F. Colyer), 837
Rosher, A. B., *Hæmophilus influenzæ* and its relation to epidemic influenza (*Pres. address*), 749
Ross, A. M., otology in school children and child welfare (*Disc.*), 108
Rowbotham, E. S., anæsthesia for abdomino-peritoneal operations for cancer of the rectum (*Disc.*), 270
  local analgesia (*Disc.*), 532

Rowbotham, E. S., shock, with special reference to anæsthesia (*Disc.*), 178
Rowley, L. J. (for D. Paterson and W. McKissock), angioma of the basal ganglia, 164
Roxburgh, A. C. (*Disc.*), 13, 247, 251, 500
Rugg-Gunn, A. (with M. Lederman), Mooren's ulcer (*By title*), 569
Rushton, M. A., regional osteitis fibrosa affecting the facial bones : two cases, 316
Russell, B. F. (*Disc.*), 247, 250, 259, 502, 706
  case for diagnosis: ? reticulosis; ? circumscribed myxœdema, 12, 258
  leucoderma and leucotrichia, 506
  morphœa guttata, 506
  (with R. M. B. MacKenna), cutaneous papillomatosis, 254
Russell, W. R., the treatment and prognosis of traumatic paraplegia (*Disc.*), 231

sacrococcygeal teratomas (R. A. Willis), 879
St. Helena, poliomyelitis on (K. I. Nissen), 923
Salisbury, Sir Edward J., the span of life (*Disc.*), 638
salpingitis, tuberculous, treatment with special reference to X-ray (E. Philipp), 376
Samuel Hyde Memorial Lecture (H. Cohen), 443
sarcoid, Boeck's, treatment with calciferol (I. R. Marre), 11
sarcoidosis (B. Green and C. W. F. McKean), 704
Saunders, C. F. (for P. Evans), hepatosplenomegaly: for diagnosis, 163
scalp, congenital defect (S. Yudkin), 533
Schlesinger, B. E., cystic disease of bone, see Burrows, N. F. E.
  diabetes insipidus, see Powell, B. W.
  nephritis with œdema, see Powell, B. W.
Schott, A., painful disability of the shoulder in coronary disease, 733
  Wolff-Parkinson-White syndrome (short P-R intervals associated with disturbances of intraventricular conduction) with attacks of paroxysmal tachycardia in an infant aged 8 months suffering from probable congenital heart disease, 472
sciatica due to disc lesions (R. H. Young), 233
sclerema (A. P. Norman), 160
sclerodactylia with œsophageal lesion (W. A. Bourne), 463
sclerosis, disseminated, ataxic nystagmus in (W. Harris), 81
  tuberose, with intracranial calcification and lesions of bone (H. Dimsdale), 81
scotoma, ring-shape, after retrobulbar neuritis (F. W. Law), 138
Scott, I. M., congenital ichthyosiform erythrodermia (Brocq), 701
Scott, L. G. (for D. Paterson), staphylococcal pneumonia with obstructive emphysema, 165
Scott, R. B., treatment of the lymphadenopathies (*Disc.*), 617
Scott, R. S. (for T. M. Bride), congenital coloboma of the iris and choroid, with cataracts, left intracapsular extraction (*By title*), 432
  infantile glaucoma in a child of 3 months—bilateral iridectomy (*By title*), 432

Scott, R. S. (for T. M. Bride), retinitis pigmentosa with bitemporal hemianopia (*By title*), 432
  right and left iridocyclitis, ? sympathetic (*By title*), 432
Scott-Brown, W. G., review of surgery of otosclerosis (*Disc.*), 327
Scowen, E. F., and Warren, F. L., biochemical aspects of over-activity of the adrenal cortex (*Disc.* on Overactivity of the adrenal cortex), 39
Sekulich, M., the present status of infectious disease control in continental Europe (*Disc.*), 632
Sellors, T. H., rehabilitation in chest injury (*Disc.*), 287
  treatment of non-tuberculous empyema (*Disc.*), 649
Semon, H. C. (*Disc.*), 10
Senear-Usher syndrome (E. C. Jones), 705
serum proteins of domestic animals (J. B. Brooksby), 187
sexual inversion, social aspects (*Discussion*), 585
Shackman, R., malignant synovioma of the left elbow, 273
Sharp, H. S., gummatous destruction of nasal septum: perforating epithelioma of nose, 284
  pemphigus of pharynx, 284
Sharpley, F. W., illumination (*Disc.*), 827
sheep, hæmatology (H. H. *Holman*), 185
shock, with special reference to anæsthesia (*Discussion*), 167
Short, R. H. D., pathology of primary or idiopathic thrombosis of the leg veins (*Disc.* on Thrombosis), 195
Shortt, H. E., kala-azar in infancy (*Disc.*), 158
shoulder, painful disability of, in coronary disease (A. Schott), 733
Shuttleworth, C. W. (with W. Harvey and C. H. LeMay), the sterilization of dental handpieces, 507
Simon, G., value of tomography in lesions of the main bronchi and their larger subdivisions (*Disc.*), 404
Simpson, J. F., congenital bilateral fistula of tea duct, one side treated by Toti's operation 286
  an operating microscope for the fenestratio operation, 320
  otology in school children and child welfar (*Disc.*), 107
Simpson, J. R., hyperkeratosis *follicularis* parafollicularis in cutem penetrar (Kyrle), 262
  (for H. J. Wallace), lichen nitidus, 9, 10
Simpson, S. L., overactivity of the adrenal cort (*Disc.*), 45
  and Taylor, J., chromophobe adenoma in male aged 67 years, 151
  and Wright, A. D., chromophobe adenoma i a male aged 15½ years, 151
sinusitis, treatment of subacute maxillary, i children (G. E. Archer), 854
skill, disorders of (D. R. Davis), 583
skin, hyperelasticity of (E. M. Kingsley-Pillers), 53
  temperature as clinical aid during anæsthesi (J. Clutton-Brock), 607

skull, Paget's disease of, with platybasia (J. Bull), 85
skulls, Romano-British, from burial-ground at Compton (Sir Frank Colyer), 837
Slot, G., thyrotoxicosis in a child aged 2 years 9 months, 159
Small, A., cirsoid aneurysm, see Priddis, K. W.
Small, M. H. (with G. B. Mitchell-Heggs), leiomyoma cutis, 249
smallpox, laboratory diagnosis (A. W. Downie), 657
Smith, A. J. D., Mooren's ulcer (*Disc.* on Radiotherapy in the treatment of non-malignant superficial eye lesions), 576
Smith, H. V., the treatment of leptomeningitis with penicillin (*Disc.* on Penicillin in neurology), 681
Smith, S. B., atypical pigmentary degeneration of the retina (*By title*), 432
Smithers, D. W., treatment of the lymphadenopathies (*Disc.*), 621
Snaith, L. M., anæsthesia for Cæsarean section (*Disc.*), 567
Sneddon, I. B., some dermatological complications of open wounds, 883
Société de Neurologie de Paris, joint meeting with Section of Neurology, 681
Solomons, B., shock, with special reference to anæsthesia (*Disc.*), 177
Sorsby, A., persistent pupillary membrane showing a network pattern (*By title*), see Reed, H.
see also Hughes, H. L.
span of life (*Discussion*), 638
Spence, A. W., pituitary infantilism with toxic goitre, 151
Spence, J. C., problems in the organization of a professorial unit (*By title*), 550
spinal cord injuries (*Discussion*), 219
Sprawson, E. C., unilateral hypoplasia of face and teeth, 835
Stanford, G. B., illumination (*Disc.*), 828
Stanley-Jones, D., the social aspects of homosexuality (*Disc.*), 588
Stannus, H. S. (*Disc.*), 273
statistics, importance of, in psychiatry (L. S. Penrose), 863
sterilization of dental handpieces (W. Harvey, C. H. LeMay and C. W. Shuttleworth), 507
Stern, D. M., stress incontinence in micturition (*Disc.*), 370
Stevenson, R. S., otology in school children and child welfare (*Disc.*), 108
the treatment of subacute maxillary sinusitis, especially in children (*Disc.*), 858
Stewart, H. H., treatment of hydronephrosis associated with abnormal vessels, 807
Stewart, M. J., the present position in regard to the pneumoconioses (*Disc.*), 783
treatment of the lymphadenopathies (*Disc.*), 621
Stewart-Wallace, A. M., cerebral œdema (*Disc.*), 697
stilbamidine, nervous complications following use of (P. Collard and S. Nevin), 87
Stirling, W., Boeck's sarcoid (*By title*), 432
stomach, neurofibroma of, in Recklinghausen's disease (T. W. Mimpriss), 120
stress incontinence in micturition (*Discussion*), 361
Sturge-Weber syndrome (N. F. E. Burrows), 546
subglottic chondroma (F. C. W. Capps), 285
surgery, orthopædic and plastic, team work in (T. P. Kilner), 892
plastic, tattooing in (D. N. Matthews), 881
swallowing, aid to, after laryngo-pharyngectomy (H. A. Kidd), 284
Symonds, Sir Charles (*Disc.*), 552, 553, 555
sympathectomy in hypertension (C. H. Wyndham), 776
synovioma, malignant, of left elbow (R. Shackman), 273
syphilis, congenital (J. Heber), 161
in eunuch (M. Critchley), 552
treatment with penicillin (*Discussion*), 811

tachycardia, paroxysmal, and Wolff-Parkinson-White syndrome in infant (A. Schott), 472
Tanner, J. M., the morphological level of personality, 301
Tanner, N. C., bone deformity associated with multiple neurofibromatosis, 47
transthoracic partial gastrectomy for intussuscepted fibromyoma of fundus of stomach, 275
two cases of transthoracic gastrectomy, 276
tattooing, technique and value in plastic surgery (D. N. Matthews), 881
Taylor, H., œsophageal carcinoma treated by resection and presternal œsophagogastrostomy, 465
Taylor, I., the present status of infectious disease control in continental Europe (*Disc.*), 623
Taylor, J. (with S. L. Simpson), chromophobe adenoma in a male aged 67 years, 151
Taylor, M., a method of recording neonatal infections in a maternity hospital (*By title*), 550
team work in orthopædic and plastic surgery (T. P. Kilner), 892
tear duct, congenital bilateral fistula (J. F. Simpson), 286
teeth, unilateral hypoplasia (E. C. Sprawson), 835
Tegner, W. S., palindromic rheumatism (*By title*), 293
psoriatic arthritis (*By title*), 293
telangiectasia, hæmorrhagic, of Rendu-Osler-Weber (C. H. Whittle), 7 (*bis*)
temporal arteritis (M. Kremer), 84
horn, deformation by tumours in middle cerebral fossa (E. Lindgren), 859
tendon transplantation for interosseous nerve paralysis (R. A. King), 272
teratomas in animals, bearings on human pathology (R. A. Willis), 635
testicle transplanted into Scarpa's triangle, survival (R. O. Ward), 810
thenar atrophy (W. R. Brain and A. D. Wright), 83
thiouracil in treatment of toxic goitre (W. R. Trotter), 610
Thomas, C. H.-, see Hamblen-Thomas, C.
Thomas, E. W. P. (*Disc.*), 12
Thomas, F. W. W.-, see Watkyn-Thomas, F. W.
Thomas, R. C., anæsthesia for Cæsarean section (*Disc.*), 557

- *Rowbotham, E. S., shock, with special reference to anæsthesia (Disc.), 178*
- Rowley, L. J. (for D. Paterson and W. McKissock), angioma of the basal ganglia, 164
- *Roxburgh, A. C. (Disc.), 13, 247, 251, 500*
- Rugg-Gunn, A. (with M. Lederman), Mooren's ulcer (*By title*), 569
- Rushton, M. A., regional osteitis fibrosa affecting *the facial bones : two cases, 316*
- Russell, B. F. (*Disc.*), 247, 250, 259, 502, 706
  - case for diagnosis: ? reticulosis; ? circumscribed myxœdema, 12, 258
  - leucoderma and leucotrichia, 506
  - morphœa guttata, 506
  - (with R. M. B. MacKenna), cutaneous papillomatosis, 254
- Russell, W. R., the treatment and prognosis of traumatic paraplegia (*Disc.*), 231

- sacrococcygeal teratomas (R. A. Willis), 879
- St. Helena, poliomyelitis on (K. I. Nissen), 923
- Salisbury, Sir Edward J., the span of life (*Disc.*), 638
- salpingitis, tuberculous, treatment with special reference to X-ray (E. Philipp), 376
- Samuel Hyde Memorial Lecture (H. Cohen), 443
- sarcoid, Boeck's, treatment with calciferol (I. R. Marre), 11
- sarcoidosis (B. Green and C. W. F. McKean), 704
- Saunders, C. F. (for P. Evans), hepatosplenomegaly: for diagnosis, 163
- scalp, congenital defect (S. Yudkin), 533
- Schlesinger, B. E., cystic disease of bone, see Burrows, N. F. E.
  - diabetes insipidus, see Powell, B. W.
  - nephritis with œdema, see Powell, B. W.
- Schott, A., painful disability of the shoulder in coronary disease, *733*
  - Wolff-Parkinson-White syndrome (short P-R intervals associated with disturbances of intraventricular conduction) with attacks of paroxysmal tachycardia in an infant aged 8 months suffering from probable congenital heart disease, 472
- sciatica due to disc lesions (R. H. Young), 233
- sclerema (A. P. Norman), 160
- sclerodactylia with œsophageal lesion (W. A. Bourne), 463
- sclerosis, disseminated, ataxic nystagmus in (W. Harris), 81
  - tuberose, with intracranial calcification and lesions of bone (H. Dimsdale), 81
- scotoma, ring-shape, after retrobulbar neuritis (F. W. Law), 138
- Scott, I. M., congenital ichthyosiform erythrodermia (Brocq), 701
- Scott, L. G. (for D. Paterson), staphylococcal pneumonia with obstructive emphysema, 165
- Scott, R. B., treatment of the lymphadenopathies (*Disc.*), 617
- Scott, R. S. (for T. M. Bride), congenital coloboma of the iris and choroid, with cataracts, left intracapsular extraction (*By title*), 432
  - infantile glaucoma in a child of 3 months—bilateral iridectomy (*By title*), 432
- Scott, R. S. (for T. M. Bride), retinitis pigmentosa with bitemporal hemianopia (*By title*), 432
  - right and left iridocyclitis, ? sympathetic (*By title*), 432
- Scott-Brown, W. G., review of surgery of otosclerosis (*Disc.*), 327
- Scowen, E. F., and Warren, F. L., biochemical aspects of over-activity of the adrenal cortex (*Disc. on Overactivity of the* adrenal cortex), 39
- Sekulich, M., the present status of infectious disease control in continental Europe (*Disc.*), 632
- Sellors, T. H., rehabilitation in chest injury (*Disc.*), 287
  - treatment of non-tuberculous empyema (*Disc.*), 649
- Semon, H. C. (*Disc.*), 10
- Senear-Usher syndrome (E. C. Jones), 705
- serum proteins of domestic animals (J. B. Brooksby), 187
- sexual inversion, social aspects (*Discussion*), 585
- Shackman, R., malignant synovioma of the left elbow, 273
- Sharp, H. S., gummatous destruction of nasal septum: perforating epithelioma of nose, 284
  - pemphigus of pharynx, 284
- Sharpley, F. W., illumination (*Disc.*), 827
- sheep, hæmatology (H. H. Holman), 185
- shock, with special reference to anæsthesia (*Discussion*), 167
- Short, R. H. D., pathology of primary or idiopathic thrombosis of the leg veins (*Disc.* on Thrombosis), 195
- Shortt, H. E., kala-azar in infancy (*Disc.*), 158
- shoulder, painful disability of, in coronary disease (A. Schott), 733
- *Shuttleworth, C. W. (with W. Harvey* and C. H. LeMay), the sterilization of dental handpieces, 507
- Simon, G., value of tomography in lesions of the main bronchi and their larger subdivisions (*Disc.*), 404
- Simpson, J. F., congenital bilateral fistula of tear duct, one side treated by Toti's operation, 286
  - an operating microscope for the fenestration operation, 320
  - otology in school children and child welfare (*Disc.*), 107
- Simpson, J. R., hyperkeratosis follicularis et parafollicularis in cutem penetrans (Kyrle), 262
  - (for H. J. Wallace), lichen nitidus, 9, 10
- Simpson, S. L., overactivity of the adrenal cortex (*Disc.*), 45
  - and Taylor, J., chromophobe adenoma in a male aged 67 years, 151
  - and Wright, A. D., chromophobe adenoma in a male aged 15½ years, 151
- sinusitis, treatment of subacute maxillary, in children (G. E. Archer), 854
- skill, disorders of (D. R. Davis), 583
- skin, hyperelasticity of (E. M. Kingsley-Pillers), 537
  - temperature as clinical aid during anæsthesia (J. Clutton-Brock), 607

Weber, F. P. (*Disc.*), 10, 118, 119, 247, 251, 252, 253, 254, 261, 476, 499, 500, 502, 533, 534, 538, 539, 546, 699, 701
Wells, G. C., recurrent ulcers of the legs, 482
  (for H. J. Wallace), keratoderma palmaris et plantaris, 9
West, M. W., intracranial hæmangioma causing convulsions (introduced by R. C. Lightwood), 164
Weston, H. C., illumination (*Disc.*), 824
Whelen, M. (with W. D. Nicol), penicillin and neurosyphilis (*Disc.* on Penicillin in neurology), 684
White, H. P. W.-, see Winsbury-White, H. P.
White, M. M., and Brain, R. T., ulcer of vulva in young girl, 243
Whitteridge, D. physiological disturbances produced by distension of the bladder (*Disc.* on The treatment and prognosis of traumatic paraplegia), 229
Whittington, T. H., the management of patients with essential hypertension (*Disc.*), 780
Whittle, C. H. (*Disc.*), 14, 250, 483, 489, 705
  case for diagnosis: ? lichen planus hypertrophicus, 7
  ? erythema multiforme, 701
  hæmorrhagic telangiectasia of Rendu-Osler-Weber, 7
  hæmorrhagic telangiectasia of Rendu-Osler-Weber with no family history, 7
  a hereditary ectodermal dysplasia, hitherto not described, including grouped comedones, 251
  ? Kaposi's varicelliform eruption, 252
  poikiloderma congenitale (Thomson); two cases, 499
  Lyell, A., and Gatman, M., Raynaud's phenomenon, with paroxysmal hæmoglobinuria, caused by cold hæmagglutination, 500
Whitworth, H. G., injured ulnar nerve (cat bite of right wrist) (*By title*), 293
whooping cough and measles, epidemiological concurrence and contrast (W. Butler), 384
Whyte, A. H., proctology past and present (*Pres. address*), 179
Wiggins-Davies, W. W. (with R. H. O. B. Robinson and T. W. Mimpriss), carcinoma of the bladder treated by local operation (*By title*), 809
  carcinoma of the prostate and carcinoma of the colon (*By title*), 809
  ectopic kidney with pyuria (*By title*), 809
  giant ureteric calculi (*By title*), 809
  hypernephroma (*By title*), 809
  intracapsular nephrectomy for recurrent renal calculi (*By title*), 809
  renal calculi (*By title*), 809
  transurethral resection in a man of 80 (*By title*), 809
  tuberculous kidney (*By title*), 809
  tuberculous kidney showing extensive calcification (*By title*), 809
  ureteric transplantation and cystectomy for carcinoma (*By title*), 809
  ureteric transplantation for obstetrical injury (*By title*), 809
Wigley, J. E. M. (*Disc.*), 245, 250, 251, 253, 482, 483
  effect of calciferol on lupus vulgaris, lupus pernio and Boeck's sarcoid (*Disc.*), 11
  exfoliative erythrodermia with marked pigmentation, 246
  impetigo herpetiformis: ? pemphigus vegetans, 248
  parapsoriasis, retiform variety, 699
Wilkinson, M. C., intertrochanteric osteotomy for the treatment of tuberculosis of the hip, 238
Willan, R. J., kidney showing calculi and tuberculosis (*By title*), 433
Willcox, J. M. (for I. Lewis), leontiasis ossea, 273
Williams, D. I. (for M. S. Thomson), granulosis rubra nasi, 499
Williams, D. J., poliomyelitis limited to both trigeminal motor nuclei, 555
Williams, E. W.-, see Watson-Williams, E.
Williams, H. G. E., stress incontinence in micturition (*Disc.*), 361
Williams, K. Ll.-, see Lloyd-Williams, K.
Williamson-Noble, F. A., illumination (*Disc.*), 827
  plastic implant into socket, 130
Willis, R. A., comments on sacrococcygeal teratomas (*Disc.* on Congenital anomalies of the anorectal region), 879
  teratomas and mixed tumours in animals and their bearings on human pathology, 635
Wilmers, M., congenital syphilis, see Heber, J.
Wilson, C. P., and McAlpine, D., glossopharyngeal neuralgia treated by trans-tonsillar section of the nerve, 82
Wilson, D. S. P.-, see Poole-Wilson, D. S.
Wilson, H. B., further experiences with curare (*Disc.*), 601
Wilson's disease (D. H. Brinton), 556
Windeyer, B. W., intrinsic cancer of the larynx: review of a series of cases (*Disc.*), 522
  Mooren's ulcer (*By title*), 569
  radiotherapy in the treatment of non-malignant superficial eye lesions (*Disc.*), 571, 577
  retinal glioma (three cases) (*By title*), 569
Winsbury-White, H. P., treatment of hydronephrosis associated with abnormal vessels (*Disc.*), 809
Wolff, E. (*Disc.*), 820
  allergy in ophthalmology (*Disc.*), 581
  dermo-lipoma (*By title*), 820
  detached retina: ? treatment, 820
  lymphoma: ? diagnosis, 820
  radiotherapy in the treatment of non-malignant superficial eye lesions (*Disc.*), 577
  result of Blaskowicz operation for congenital ptosis (*By title*), 820
Wolff-Parkinson-White syndrome in infant of 8 months (A. Schott), 472
Woodman, E. M. (*Disc.*), 285
Woolmer, R., shock, with special reference to anæsthesia (*Disc.*), 177
Worster-Drought, C. (*Disc.*), 83, 84
  penicillin in neurology (*Disc.*), 683
wounds, dermatological complications of open (I. B. Sneddon), 883
Wright, A. D. (*Disc.*), 83, 122
  the management of patients with essential hypertension (*Disc.*), 774, 780

Thomson, M. S. (*Disc.*), 9, 482, 483, 500
  erythematous initial tuberculide (*Disc.*), 257
  granulosis rubra nasi, see Williams, D. I.
Thorne-Thorne, B., radiotherapy in the treatment of non-malignant superficial eye lesions (*Disc.*), 577
threadworms, diagnosis (J. M. Watson and R. C. MacKeith), 539
thrombophlebitis retinæ (T. K. Lyle), 818
thrombosis (*Discussion*), 193
  femoral, with pulmonary infarction, ligation of inferior vena cava (J. D. Fergusson), 49
Thrower, W. R., the ætiology of chronic rheumatism (*Disc.*), 345
thyroid, carcinoma of (J. M. Graham and R. McWhirter), 669
thyrotoxicosis in child 2 years 9 months old (G. Slot), 159
Tippett, G. O., cyst in the femur, 485
  diaphyseal aclasis, 485
Tizard, J. P. M. (for D. Paterson), hepatosplenomegaly, 538
Todd, R. M., traumatic periostitis, 535
tomography, value in bronchial lesions (S. Nowell), 399
tongue, cancer of, treatment (*Discussion*), 409
torticollis, ocular (T. K. Lyle), 819
toxoplasmosis, two cases (A. Franceschetti), 821
tracers, radioactive (*Discussion*), 354
trachoma, Denig's operation for (N. Pines), 129, 139, 569
trapezio-metacarpal joint, osteo-arthritis, treated by excision (W. H. Gervis), 492
Trevor, D., abnormal ossification in scapular region (*By title*), 885
trigeminal neuropathy following stilbamidine (P. Collard and S. Nevin), 87
tropical lichenoid dermatitis (H. J. Wallace), 502
Trotter, W. R. (*Disc.*), 704
  the treatment of toxic goitre by thiouracil (*Disc.* on The treatment of toxic goitre), 610
Troup, W. A., the ætiology of chronic rheumatism (*Disc.*), 345
tuberculide, erythematous initial (W. J. Hohmann), 255
  multiple (H. W. Barber), 245
  papulo-necrotic (L. Forman), 248
tuberculous abscess following penicillin therapy (P. J. Coope), 161
Tucker, W. E., pain in the upper limb, excluding shoulder lesions (*Disc.*), 498
Tuckwell, E. G., the concentration of penicillin in bile, 654
Tumarkin, A., transmeatal attico-antrotomy in chronic tympanomastoid suppuration, 761, 772
tumours, mixed, in animals, bearings on human pathology (R. A. Willis), 635
Turner, J. W. A. (*Disc.*), 88
  pain in the upper limb, excluding shoulder lesions (*Disc.*), 498
tympanomastoid suppuration, attico-antrotomy in (A. Tumarkin), 761
typhoid osteitis of long bones (E. T. Bailey), 486

ulcer, recurrent, of legs (G. C. Wells), 483
  rodent, treated by radiotherapy (J. A. C. Fleming), 469
ulna, osteoid-osteoma of upper end (D. Wainwright), 487
urethra, injuries (D. S. Poole-Wilson), 798
urinary incontinence, stress (*Discussion*), 361
urology, penicillin in (*Discussion*), 433
uterus, rupture (I. Donald), 379

? varicelliform eruption, Kaposi's (C. H. Whittle), 252
venereal disease control in Denmark, Sweden and British-occupied Germany (F. R. Curtis), 630
Vernon, H. K., leiomyoma of bladder treated by cystectomy (*By title*), 433
  see also Desmond, A. M.
vertebræ, cervical, injuries of (V. H. Ellis), 19
Vessell, V. E., anæsthesia for abdomino-peritoneal operations for cancer of the rectum (*Disc.*), 269
Vincent, C., cerebral œdema (*Disc.*), 689
Vine, J. M., malaria control with D.D.T. on a national scale—Greece, 1946, 841
virus infections, laboratory diagnosis of (*Discussion*), 657
Vlasto, M., anterior ethmoidal hæmorrhage (*Disc.*), 283
vulva, ulcer of, in young girl (M. M. White and R. T. Brain), 243

Wainwright, D., osteoid-osteoma of upper end of ulna, 487
  recurrent dislocation of the elbow-joint, 885
Welford, A. S. H., otology in school children and child welfare (*Disc.*), 106
Walker, D. G., severe infections of the mandible, 309
Walker, V., allergy in ophthalmology (*Disc.*), 582
Wallace, A. M. S.-, see Stewart-Wallace, A. M.
Wallace, H. J., case for diagnosis: ? lichen sclerosus, 8
  keratoderma palmaris et plantaris, see Wells, G. C.
  lichen nitidus, see Simpson, J. R.
  tropical lichenoid dermatitis, 502
Walsh, J. W. T., illumination (*Disc.*), 822
Ward, R. O., survival of a testicle transplanted into Scarpa's triangle, 810
Warner, E. C., dermatomyositis, see Clarke, W. E.
Warren, F. L. (with E. F. Scowen), biochemical aspects of over-activity of the adrenal cortex (*Disc.* on Overactivity of the adrenal cortex), 39
Waterlow, J. C., nutritional liver disease in West Indian infants, 347
Watkyn-Thomas, F. W., transmeatal attico-antrotomy in chronic tympanomastoid suppuration (*Disc.*), 771
Watson, J. M., and MacKeith, R. C., diagnosis of threadworms (*Demonst.*), 539
Watson-Williams, E., anterior ethmoidal hæmorrhage (*Disc.*), 283

Wright, A. D., von Recklinghausen's disease, 49
  total gastrectomy with œsophagoduodenal anastomosis, 50
  (with W. R. Brain), compression neuritis of both median nerves in the carpal tunnel: surgical decompression; Klippel-Feil deformity of neck; Sprengel shoulder, 83
  (with S. L. Simpson), chromophobe adenoma in a male aged 15½ years, 151
Wright, H., blood findings (*Disc.* on Thrombosis), 197
Wright, J., modern methods in the control of airborne infections (*Disc.*), 382
Wyllie, W. G., exophthalmic goitre, see Alexander, J. M.
  neurofibromatosis, see Alexander, J. M.
  precocious puberty of ? suprarenal origin, see Burrows, N. F. E.
  primary hyperplasia of the parathyroids in a boy aged 8 years, see Burrows, N. F. E.
Wyllie, W. G., pseudo-hypertrophic muscular dystrophy, see Alexander, J. M.
  Sturge-Weber syndrome, see Burrows, N. F. E.
Wyndham, C. H., sympathectomy in hypertension (*Disc.* on The management of patients with essential hypertension), 776

xanthomatosis (C. P. Petch), 118
X-ray treatment of inflammatory diseases (*Discussion*), 109
  of tuberculous salpingitis (E. Philipp), 376

Young, G., otology in school children and child welfare (*Disc.*), 107
Young, R. H., protrusion of intervertebral discs, 233
Yudkin, S., spontaneous bilateral pneumothorax occurring in a premature baby during the neo-natal period, see Paul, J. W.
  (for H. M. M. Mackay), congenital defect of the scalp, 533

Printed by Staples Press Limited at their Great Titchfield Street, London, establishment.